Long-Term Arrhythmia-Free Survival in Patients with Severe Left Ventricular Dysfunction and No Inducible Ventricular Tachycardia Post Myocardial Infarction

Running title: Zaman et al.; Arrhythmia-free survival post-MI if no inducible VT

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Abstract

Background—A negative electrophysiology study (EPS) may delineate a sub-group of patients with severely impaired left ventricular ejection fraction (LVEF) who are safe long-term without an implantable-cardioverter defibrillator (ICD).

Methods and Results—Consecutive patients treated with primary percutaneous coronary intervention for ST-elevation myocardial infarction (STEMI) underwent early (median 4 days) LVEF assessment. Patients with LVEF ≤40% underwent EPS. A prophylactic ICD was implanted for a positive [inducible monomorphic ventricular tachycardia (VT)] but not a negative (no inducible VT or inducible ventricular fibrillation (VF)/flutter) EPS result. Patients who would have become eligible for a late primary prevention ICD with LVEF ≤30% or ≤35% with NYHA class II/III heart failure (HF) were included and analysed according to EPS result. Patients with LVEF >40%, ineligible for EPS, were followed as controls (n=1,286). The primary endpoint was survival free of death or arrhythmia (resuscitated cardiac arrest or sustained VT/VF). EPS performed in 128 patients with LVEF ≤30%/≤35% & HF was negative in 63% (n=80) and positive in 37% (n=48). ICDs were implanted in <0.1%, 4% and 90% of control, EPS-negative and EPS-positive patients, respectively. The distribution of time to death or arrhythmia was comparable in control patients and EPS-negative patients with LVEF ≤30%/≤35% & HF (P=0.738); who both differed significantly from EPS-positive patients (P<0.001). At 3 years 91.8±3.2%, 93.4±1.0% and 62.7±7.5% of control, EPS-negative and EPS-positive patients were free of death or arrhythmia, respectively.

Conclusions—Re-vascularised STEMI patients with severely impaired LV function but no inducible VT have favourable long term prognosis without the protection of an ICD.

Key words: myocardial infarction; tachyarrhythmias; electrophysiology; death, sudden
Introduction

Impaired left ventricular ejection fraction (LVEF) is one of the strongest predictors of death or arrhythmia post-myocardial infarction (MI). Randomised trials have demonstrated that post-MI patients with impaired LVEF derive a mortality benefit with implantation of a prophylactic implantable-cardioverter defibrillator (ICD) for prevention of sudden cardiac death (SCD).\(^1,2\)

This mortality benefit is seen only in the chronic stage, with no randomised trial yet showing a benefit of early post-MI (within 40 days) ICD implantation.\(^3,4\) Current guidelines therefore limit prophylactic ICDs to patients who are >40 days post-MI with either LVEF ≤30% or LVEF ≤35% in the presence of New York Heart Association (NYHA) class II/III heart failure (HF).\(^5\)

However, this risk stratification method for prevention of SCD is limited by the poor specificity of impaired LVEF for arrhythmic versus non-arrhythmic cardiac death.\(^6\) In addition, while the rate of SCD has declined in the era of early revascularisation for MI, it remains concerningly elevated in the first 40 days.\(^7,8,9\) Inducible ventricular tachycardia (VT) at electrophysiological study (EPS) demonstrates the presence of a substrate for re-entrant tachyarrhythmia and consistently predicts arrhythmia in observational and randomised studies.\(^10-16\) The potential utility of EPS to guide early ICD implantation post-MI has been demonstrated.\(^17,18\) While EPS has been shown to select patients at high risk of future tachyarrhythmia, concern still surrounds its negative predictive value. We aimed to demonstrate that early post-MI patients with severe LV dysfunction and a negative EPS (no inducible VT) are safe long-term, without the protection of an ICD.

Methods

Consecutive patients with ST-elevation myocardial infarction (STEMI) treated with primary
percutaneous coronary intervention (PPCI) at a single tertiary centre from 2004-2011 were prospectively recruited. The study was approved by an institutional review committee and the subjects gave their written informed consent. Patients presented directly to the intervention-capable Westmead Hospital or were referred by three associated district hospitals. All patients in the study had angiographically-confirmed STEMI. No patients received thrombolytic therapy. Patients with STEMI underwent inpatient assessment of LV function at day 3 or later post-MI with gated heart pool scan (GHPS) or transthoracic echocardiogram (TTE) where GHPS was not available. Following early revascularization, patients with LV dysfunction were commenced on optimal medical therapy including beta-blockers, ACE-I, statins and anti-platelet therapy. According to hospital protocol patients with LVEF $\leq 40\%$ were eligible for EPS as a risk stratification test to identify patients at risk of SCD. Previous research conducted at our institution analyzing the predictive value of EPS post-STEMI prospectively recruited patients from 1999-2008$^{17, 18}$ with $\sim 40\%$ of these patients included in the current study. In this study patients were included if they had an EPS performed with LVEF $\leq 30\%$ (irrespective of the presence of heart failure) or an EPS performed with LVEF 31-35% (only if heart failure NYHA class II or III was also present). Patients with a LVEF $> 40\%$ who were not eligible for EPS were followed as the control group.

**Electrophysiologic Study (EPS)**

Programmed stimulation was performed at twice diastolic threshold at the right ventricular apex (single site) using a programmable stimulator. A drive train (S1S1) of 8 beats at 400ms was followed by up to 4 extrastimuli. Stimuli were rectangular pulses of 2 ms duration at twice diastolic threshold with a 3 s delay between each drive train. The initial ES was delivered at a coupling interval of 300ms and then decreased in 10ms steps to ventricular refractoriness. If the
earliest possible ES (e.g. S1S2) failed to induce VT, that ES was delivered 10 ms outside the ventricular effective refractory period and an additional ES added (e.g. S2S3) at a coupling interval of 300 ms. The additional ES was decreased in 10 ms steps in the same manner. Additional ES were added in a similar manner (always starting with coupling interval of 300 ms) until either VT or VF was induced or refractoriness of the fourth ES was reached. There was no set lower limit for the shortest permissible ES coupling interval. The programmed stimulation was repeated a second time from the same site, using the same protocol, if the initial induction was negative for VT. Isoprenaline infusion was not utilized to facilitate VT induction. Patients with sustained monomorphic VT cycle length (CL)≥200ms with up to 4 extra-stimuli were considered inducible (positive EPS). Inducible VT had to be at least 30 seconds in duration if hemodynamically tolerated or at least 10 seconds in duration if hemodynamically unstable. Patients with no arrhythmia induced or inducible VF or ventricular flutter (CL<200ms) were considered to have a negative EPS. The predictive value of this approach has been discussed in detail previously.17-22 Pre-discharge ICD implantation was recommended for EPS positive patients. EPS negative patients were discharged without an ICD and according to study protocol did not undergo ICD implantation >40 days post-MI irrespective of persistent LV dysfunction.

**ICD Implantation and Programming**

All devices were pre- or sub-pectoral systems with the manufacturer and type determined by the hospital device acquisition process. Device detection and therapy were programmed as follows: VF required 18 out of 24 R-R intervals with CL<250ms. Therapy was a single ATP burst during charging (8 pulses per burst) followed by up to 6 shocks. VT required 16 consecutive beats with CL 251-360ms and 12 consecutive beats with CL 251-360ms for re-detection. Initial therapy for VT was up to three ATP bursts (8 pulses per burst) followed by up to 6 shocks. Ventricular
arrhythmia that did not reach the set number of detection intervals was classified as non-sustained. Discriminators for supraventricular tachycardia were standardised based on arrhythmia onset, stability and ventriculoatrial dissociation. To reduce unnecessary right ventricular pacing, backup pacing was set at 40bpm VVI for single chamber devices and AAI-DDD for devices with an atrial lead.

**Endpoints and Follow Up**

The primary endpoint was a combination of all-cause death and arrhythmia. Secondary endpoint was the first arrhythmic event (arrhythmia defined as SCD, resuscitated cardiac arrest and ECG documented sustained VT or ventricular fibrillation). Cause of death was determined by two local investigators based on information obtained from witnesses, family members, death certificates provided by the state registry of births and deaths, hospital medical records, rhythm strips and autopsy reports. A third independent investigator adjudicated if opinion differed. Sudden cardiac death was strictly defined based on a modified Hinkle and Thaler system\(^23\) as death that occurred “suddenly and unexpectedly” in a patient in otherwise stable condition, inclusive of witnessed instantaneous death (with or without documentation of arrhythmia), unwitnessed death if the patient had been seen within 24 hours before death (in the absence of another clear cause of death), death caused by incessant ventricular tachyarrhythmia, deaths considered a sequel of cardiac arrest and death resulting from pro-arrhythmia of anti-arrhythmic drugs. Resuscitated cardiac arrest was defined as a sudden circulatory arrest requiring cardiopulmonary resuscitation with the most likely cause a tachyarrhythmia (with or without documented VT or VF) from which the patient regains consciousness. Ventricular tachyarrhythmia was defined as ECG-document VT or VF in patients without an ICD, or ICD-detected VT or VF which required treatment to terminate (anti-tachycardia pacing or shock).
Cardiac mortality included both sudden and non-sudden cardiac deaths with non-sudden cardiac deaths defined as death due to myocardial infarction, heart failure or another cardiovascular cause. Heart failure was defined as symptoms or signs consistent with congestive heart failure (either clinical or radiographic evidence) requiring treatment with decongestive therapy (diuretics or inotropes), intra-aortic balloon pump or invasive/non-invasive ventilation. Only heart failure during the index STEMI admission was assessed. All patients were followed by the study investigators throughout their time in hospital and by telephone contact at 1, 3 and 6 months after discharge with 6-monthly intervals thereafter. Patients with an ICD were also followed in the ICD clinic with electrograms of device detections or activations analyzed by the study investigators.

**Statistical Analysis**

SPSS for Windows (release 21.0) was used to analyse the results. Patients were analysed according to study group assignment. All analyses were exploratory and two-tailed tests with a significance level of 5% were used throughout. No adjustment has been made for multiple comparisons. False positive findings are therefore possible and any statistically significant results need to be confirmed in further independent studies. Chi-squared or Fisher’s exact tests as appropriate were used to test for association between categorical variables. Analysis of variance or Kruskal-Wallis equivalent were used to test for differences in the distribution of continuous variables between the groups. Kaplan-Meier curves were used to illustrate the cumulative distribution of the primary endpoint by time post-infarction. Tarone-Ware tests were used to look for differences in survival distribution between the groups.
Results

A total 1,910 STEMI patients were taken to the cardiac catheterisation lab for PPCI. Of these patients, 188 (9.8%) did not undergo early LVEF assessment. The reasons for this included in-patient death prior to LVEF assessment (n=94, 50%), patient refusal or discharge prior to LVEF assessment (n=54, 29%), transfer back to peripheral hospital (n=20, 11%) and transfer to another treating specialty (n=20, 11%). Early LVEF assessment was performed in 1,722 patients at a median of 4 days post-STEMI by gated heart pool scan in 87% (n=1,506), TTE in 12% (n=212) and sestamibi scan or TOE in 1% (n=4). Patients with LVEF>40% made up 75% (n=1,286) of STEMI patients and formed the control group. Of the total cohort 10% of patients had LVEF≤30% (n=172), while 8% had a LVEF 31-35% (n=136), of which 38% (n=51) had concomitant NYHA class II/III HF. EPS was performed at a median 8 [lower quartile to upper quartile 6-11] days post-STEMI in 57% (n=128) of patients with LVEF≤30% or ≤35% & HF (n=223). It was not performed in all patients due to either in-hospital death prior to EPS (n=39, 41%), secondary indication for ICD (n=9, 9%), patient refusal (n=5, 5%) or patient deemed inappropriate for ICD implantation due to limited life-expectancy (old age, significant co-morbidities or malignancy, n=42, 44%). Of patients with LVEF≤30% or ≤35% & HF the EPS was negative in 63% (n=80) and positive for inducible VT in 37% (n=48). The baseline characteristics according to the three study groups are shown in Table 1.

ICD Implantation

A pre-discharge ICD was implanted early (median 13 days) post-STEMI in 43/48 (90%) patients with LVEF≤30% or ≤35% & HF and a positive EPS. An ICD was not implanted in 5 patients with a positive EP study due to patient refusal (n=2) and patient not covered by health insurance (n=3). A pre-discharge ICD was implanted in 3/80 (4%) patients with a negative EPS (protocol
violations) by treating physicians based on impaired LVEF alone. A pre-discharge ICD was implanted in <0.1% of control patients (LVEF>40%) due to a secondary indication (n=1).

**Primary Outcome**

Median follow-up for all patients was 32 (lower quartile to upper quartile 24-50) months. Median follow-up for EPS negative patients with LVEF≤30%/≤35% & HF was 42 (lower quartile to upper quartile 24-61) months. The Kaplan-Meier estimated survival free of death or arrhythmia is shown in **Figure 1** with no significant difference between patients in the control group (LVEF>40%) versus patients with LVEF≤30%/≤35% & HF who were EPS negative (P=0.738). At 3 years 93.4±1% and 91.8±3.2% of patients with LVEF≤30%/≤35% & HF & negative EPS and control patients (LVEF>40%) were free of death or arrhythmia, respectively. The Kaplan-Meier survival plot inclusive of EPS positive patients is shown in **Figure 2** with EPS positive patients having a significantly lower survival free of arrhythmia or death compared to control (P<0.001) and EPS negative patients (P<0.001). At 3 years 62.7±7.5% of EPS positive patients were free of arrhythmia or death.

**Secondary Outcomes**

Over the follow-up period arrhythmia occurred in <1% (n=6) of control patients (LVEF>40%), 2.5% (n=2) of EPS negative patients and 33% (n=16) of EPS positive patients (1 SCD in an EPS positive patient without an ICD due to protocol violation). Two-year arrhythmic event rates were 1% for EP negative (n=1) and 24% for EP positive patients (n=11). The sensitivity and specificity of EPS at 2 years was therefore 92% and 68%, respectively. There was no significant difference in the Kaplan-Meier estimated total mortality in control, EPS negative and EPS positive patients, respectively (P=0.451). At 3 years the total mortality was 6.5±1%, 6.8±2.9% and 14.6±5.5% in control, EPS negative and EPS positive patients, respectively. Death and
arrhythmia outcomes are expanded in Table 2. Inappropriate ICD activations (all due to supraventricular tachycardia) occurred in 11% of patients with an ICD (5/47) with one patient receiving an inappropriate shock.

Discussion

Post-MI patients with severe LV dysfunction have low long-term rates of arrhythmia or death if no VT is induced at electrophysiology testing. Patients with LVEF>40% were followed as a control group given the well established low risk of SCD or arrhythmia in this population.12, 14, 24 We found that EPS negative patients with severe LV dysfunction had a similarly good long-term prognosis as patients with preserved LVEF.

It is well accepted that the presence of inducible monomorphic VT at EPS selects patients at high risk for spontaneous tachyarrhythmia. However, a predominant concern with EPS as a risk stratification tool for prevention of SCD is its negative predictive value. Results from the MADIT II trial suggested that EPS added little prognostic information, as they found patients late post-MI with LVEF≤30% experienced sudden death even if EP testing was negative.1 The more recent CARISMA and ABCD trial, found that while EPS had the highest specificity, its sensitivity was comparable to non-invasive modalities such as microvolt T-wave alternans and heart rate variability. However, the negative predictability of EPS appears critically dependent on the VT induction protocol used. The MADIT-II study performed EPS through the ICD device in a proportion of patients which would have considerably restricted its predictive ability. The ABCD and CARISMA investigators used an EP protocol of up to 3 extrastimuli and included not only sustained monomorphic VT as a positive result, but VF or polymorphic VT. Inducible VF or ventricular flutter cycle length <200ms has been shown to be a non-predictive result.19, 25 We
have previously demonstrated that a VT induction protocol containing four extrastimuli, with inducible monomorphic VT cycle length >200ms classified as a positive result best identifies nearly all patients at high risk of arrhythmia. However, they excluded all deaths within one year. The current study which utilised such a VT induction protocol strongly suggests that patients with a negative EPS have very low rates of death or arrhythmia despite having severe LV dysfunction and no ICD.

The evidence supporting post-MI ICD implantation for primary prevention has largely come from randomised trials utilising LVEF as the sole selection tool. However, LVEF used alone has low specificity for arrhythmic versus non-arrhythmic deaths and limited sensitivity whereby a large proportion of SCDs occur above the LVEF cut-off. The MADIT-II and SCD-HeFT trials which used LVEF alone found a large number (11 and 14, respectively) required treatment with a defibrillator to save one life. The risks of ICD implantation such as multiple or inappropriate shocks and quality of life deterioration, must be weighed against potential survival benefits. In addition, ICDs are expensive, and a cost-benefit ratio should be considered. In comparison, the MUSTT and MADIT trials where EPS was used in addition to LVEF, only 4 and 5 patients required treatment with an ICD to save one life. Our findings suggest that within the sub-group of post-MI patients with LVEF≤35%, low-risk patients exist who would derive little benefit from an ICD. Restricting ICD implantation in this group through the additional use of EPS could allow a substantial cost benefit without a sacrifice in population life expectancy.

Depressed left ventricular function is a strong predictor of mortality. In randomised ICD trials the mortality in patients with LVEF≤30% was high, with 1 year mortality ranging from 6.8-19%. Studies assessing mortality and arrhythmia in the cohort of patients treated exclusively with PPCI are limited. Ottervanger et al in 2007 described a much lower rate of death post PPCI for STEMI of 5.8% at 1 year. However, they excluded all deaths within one
month, and LVEF was measured later after MI. Sudden death was the most common cause of
death at 40%. Total mortality in the current study in patients with LVEF ≤30% or ≤35% & HF
who survived to undergo EPS-guided ICD implantation was low at 10% at 3 years. This likely
reflects the improved mortality in the era of early revascularisation for STEMI, optimal medical
management and targeted ICD implantation.

Limitations
The main limitation of this study was its observational nature. As ICDs were not implanted in
EP-negative patients there was an unavoidable bias in the detection of arrhythmic events in EP
positive patients. ICD-detected VT/VF overestimates SCD by two to four fold29 which limits any
collection in arrhythmic events of overall EP positive with overall EP negative patients
(although the very low SCD rate of <1% in the EP negative group is reassuring). However, the
primary aim of this study to compare survival in EP negative to control patients (LVEF>40%)
was not influenced by this bias, as both groups did not receive ICDs as per our study protocol.
While we have demonstrated that there was no significant difference between EP negative
patients with impaired LVEF, and control patients with LVEF>40% we have not proven these
groups are equivalent. To demonstrate a statistically significant equivalence to within 1% in
survival free of arrhythmia or death between EP negative and control patients, several thousand
patients would be needed in each arm. Confirmation of an EPS-guided primary prevention of
SCD strategy requires a large multicentre randomised controlled trial.

Conflict of Interest Disclosures: None.
References:


### Table 1. Baseline Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LVEF≤30% or ≤35% &amp; HF</th>
<th>Control LVEF&gt;40%</th>
<th>P-value*</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EP–ve (n=80)</td>
<td>EP+ve (n=48)</td>
<td>P-value*</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean±SD</td>
<td>58±12</td>
<td>57±12</td>
<td>0.461</td>
<td>59±12</td>
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<tr>
<td>Male gender</td>
<td>79%</td>
<td>92%</td>
<td>0.044</td>
<td>80%</td>
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<td>Background history:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior IHD</td>
<td>21%</td>
<td>34%</td>
<td>0.072</td>
<td>22%</td>
</tr>
<tr>
<td>Hypercholesteraemia</td>
<td>47%</td>
<td>66%</td>
<td>0.028</td>
<td>57%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39%</td>
<td>51%</td>
<td>0.134</td>
<td>54%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>16%</td>
<td>34%</td>
<td>0.014</td>
<td>23%</td>
</tr>
<tr>
<td>Smoker, past or current</td>
<td>71%</td>
<td>75%</td>
<td>0.396</td>
<td>68%</td>
</tr>
<tr>
<td>LAD-related anterior STEMI</td>
<td>87%</td>
<td>73%</td>
<td>0.079</td>
<td>34%</td>
</tr>
<tr>
<td>STEMI treatment:</td>
<td></td>
<td></td>
<td></td>
<td>0.391</td>
</tr>
<tr>
<td>PCI/Stenting</td>
<td>99%</td>
<td>94%</td>
<td>0.094</td>
<td>96%</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>4%</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>Medical management only</td>
<td>1%</td>
<td>2%</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>Post Procedure TIMI III flow</td>
<td>99%</td>
<td>89%</td>
<td>0.026</td>
<td>96%</td>
</tr>
<tr>
<td>Heart Failure during STEMI admission</td>
<td>54%</td>
<td>71%</td>
<td>0.041</td>
<td>10%</td>
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<td>Discharge Pharmacotherapy:</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ACE-I or ARB</td>
<td>87%</td>
<td>81%</td>
<td>0.244</td>
<td>89%</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>96%</td>
<td>83%</td>
<td>0.016</td>
<td>86%</td>
</tr>
<tr>
<td>Statin</td>
<td>99%</td>
<td>85%</td>
<td>0.004</td>
<td>98%</td>
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<tr>
<td>Aspirin</td>
<td>100%</td>
<td>100%</td>
<td>-</td>
<td>100%</td>
</tr>
<tr>
<td>Clopidogrel or Prasugrel</td>
<td>96%</td>
<td>91%</td>
<td>0.153</td>
<td>98%</td>
</tr>
<tr>
<td>LVEF, mean±SD</td>
<td>27±5%</td>
<td>26±6%</td>
<td>0.340</td>
<td>54±8%</td>
</tr>
</tbody>
</table>

*P-value comparison between EP negative and EP positive patients. †P-value comparison between EP negative and control patients.

LVEF=left ventricular ejection fraction; HF=heart failure; EP–ve=electrophysiology study negative; EP+ve=electrophysiology study positive; IHD=ischaemic heart disease; STEMI=ST-elevation myocardial infarction; PCI=percutaneous coronary intervention; CABG=coronary artery bypass grafting; TIMI=Thrombolysis in Myocardial Infarction flow score; ACE-I=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker.
Table 2. Mortality and Arrhythmia Outcomes.

<table>
<thead>
<tr>
<th>Outcome (Number, %)</th>
<th>Total (n=1,414)</th>
<th>LVEF≤30%/≤35%&amp;HF</th>
<th>P-value*</th>
<th>Control LVEF&gt;40% (n=1,286)</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Non-sudden cardiac death</td>
<td>106, 7%</td>
<td>6, 8%</td>
<td>6 , 13%</td>
<td>0.334</td>
<td>94 , 7%</td>
</tr>
<tr>
<td>- Sudden cardiac death</td>
<td>44</td>
<td>4</td>
<td>1</td>
<td></td>
<td>39</td>
</tr>
<tr>
<td>- Non cardiac</td>
<td>55</td>
<td>1</td>
<td>3</td>
<td></td>
<td>51</td>
</tr>
<tr>
<td>Total arrhythmic events:</td>
<td>24, 2%</td>
<td>2, 3%</td>
<td>16, 33%</td>
<td>&lt;0.001</td>
<td>5, 1%</td>
</tr>
<tr>
<td>- Sudden cardiac death</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>- Cardiac arrest or VT/VF without an ICD</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>- ICD-treated VT/VF</td>
<td>14</td>
<td>0</td>
<td>13</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Events up to 40 days post-STEMI (%= proportion of total events):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cardiac death</td>
<td>18, 35%</td>
<td>1, 20%</td>
<td>2, 67%</td>
<td>15, 35%</td>
<td></td>
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<tr>
<td>- Total arrhythmia</td>
<td>7, 29%</td>
<td>0</td>
<td>5, 30%</td>
<td>2, 33%</td>
<td></td>
</tr>
<tr>
<td>Proportion of patients alive and free of arrhythmia or death</td>
<td>1284, 91%</td>
<td>73, 91%</td>
<td>29, 60%</td>
<td>&lt;0.001</td>
<td>1,190, 93%</td>
</tr>
</tbody>
</table>

*Tarone-Ware p value comparison between EP-negative and EP-positive patients. †Tarone-Ware p value comparison between EP-negative and control patients. LVEF=left ventricular ejection fraction; HF=heart failure; EP-ve=electrophysiology study negative; EP+ve=electrophysiology study positive; VT=ventricular tachycardia; VF=ventricular fibrillation; STEMI=ST-elevation myocardial infarction.
Figure Legends:

**Figure 1.** Kaplan-Meier survival free of death or arrhythmia (cardiac arrest or VT/VF) for patients with severe LV dysfunction but a negative EPS (no inducible VT), compared to control (LVEF>40%).

**Figure 2.** Kaplan-Meier survival free of death or arrhythmia in patients with severe LV dysfunction and a negative (no inducible VT) versus positive (inducible VT) EPS. Panel (A) arrhythmia is inclusive of ICD-treated VT events and Panel (B) arrhythmia is exclusive of ICD-treated VT events.
Figure 1

**Survival Free of Death or Arrhythmia (%)**

- **LVEF > 40%** (Control, n=1,286)
- **LVEF ≤ 30% ≤ 35% & HF**
- **No Inducible VT**

**P = 0.738**

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Time from ST-Elevation MI (months)</th>
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<td>LVEF &gt; 40%</td>
<td>1286</td>
</tr>
<tr>
<td>LVEF ≤ 35% EP-ve</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>912</td>
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<td>57</td>
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<td></td>
<td>31</td>
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Figure 2
Long-Term Arrhythmia-Free Survival in Patients with Severe Left Ventricular Dysfunction and No Inducible Ventricular Tachycardia Post Myocardial Infarction
Sarah Zaman, Arun Narayan, Aravinda Thiagalingam, Gopal Sivagangabalan, Stuart Thomas, David L. Ross and Pramesh Kovoor

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