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Original Article

Identifying high risk patients post myocardial infarction with reduced left ventricular function using loop recorders INSPIRE-ELR clinical study

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ABSTRACT

Aims: Sudden cardiac death (SCD) continues to be a devastating complication amongst survivors of myocardial infarction (MI). Mortality is high in the initial months after MI. The aims of the INSPIRE-ELR study were to assess the proportion of patients with significant arrhythmias early after MI and the association with mortality during 12 months of follow-up.

Methods: The study included 249 patients within 14 days after MI with left ventricular ejection fraction (LVEF) $\leq$35% at discharge in 11 hospitals in India. Patients received a wearable external loop recorder (ELR) 5 $\pm$ 3 days after MI to monitor arrhythmias for 7 days.

Results: Patients were predominantly male (86%) with a mean age of 56 $\pm$ 12 years. In 82%, reperfusion had been done and all received standard of care cardiovascular medications at discharge. LVEF was 32.2 $\pm$ 3.9%, measured 5.1 $\pm$ 3.0 days after MI. Of the 233 patients who completed monitoring (7.1 $\pm$ 1.5 days), 81 (35%) experienced significant arrhythmias, including Ventricular Tachycardia/Fibrillation (VT/VF): 10 (4.3%); frequent Premature Ventricular Contractions (PVCs): 65 (28%); Atrial Fibrillation (AF): 8 (3.4%); chronic atrial flutter: 4 (1.7%); 2nd or 3rd degree Atrioventricular (AV) block: 4 (1.7%); and symptomatic bradycardia: 8 (3.4%). In total, 26 patients died. Mortality was higher in patients with clinically significant arrhythmia (at 12 months: 23.6% vs 4.8% with 19 vs 7 deaths, hazard ratio (HR) = 5.5, 95% confidence interval (CI) 2.3 to 13.0, $p < 0.0001$). Excluding 7 deaths during ELR monitoring, HR = 4.5, $p < 0.001$.

Conclusion: ELR applied in patients with acute MI and LV dysfunction at the time of discharge identifies patients with high mortality risk.

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1. Introduction

Due to the improvement in treatment modalities and adherence to guidelines-based therapy, the mortality of acute Myocardial Infraction (MI) has declined.[1] However sudden cardiac death (SCD) continues to be a devastating complication amongst survivors of MI. The risk of SCD is highest during the first month after MI and declines over time and has been independently associated with heart failure but not with recurrent ischemia.[2] The Valsartan in Acute Myocardial Infarction Trial (VALIANT) study reported a 2–2.5-fold higher risk of SCD in first 90 days after MI in patients with Left Ventricular (LV) dysfunction.[3]

Despite the fact that the incidence of SCD is the highest in the first month after MI; the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) trial did not show benefit of Implantable Cardioverter Defibrillator (ICD) placement less than 40 days after an MI in those with low left ventricular ejection fraction (LVEF).[4] As result of which the guidelines recommend ICD be offered only to patients at least 40 days post MI and 90 days post revascularization leaving the population of patients within 40–90 days of MI and low LVEF exposed to the risk of sudden death.[5]

Determining the risk of sudden death after MI continues to be challenging. The present study sought to identify arrhythmias in patients discharged after acute MI with low LVEF detected at discharge and then at 8–10 weeks after discharge using a wearable external loop recorder (ELR). Since there are dynamic changes in LV remodeling after treatment of MI, it was thought important to observe the changes in arrhythmias and LVEF again at 8–10 weeks. The aim of this study was to understand if arrhythmia monitoring at these 2 intervals could predict 1-year mortality in patients with acute MI and a low LVEF at discharge.

2. Methods

The Identifying High Risk Patients Post Myocardial Infarction with Reduced Left Ventricular Function using External Loop Recorders (INSPIRE-ELR) study was a prospective, multicenter, non-randomized study conducted in India.

Patients who had been diagnosed with acute MI (STEMI or non-STEMI), documented within 10 days of onset, with LVEF $\leq$35% as measured by echocardiography (Simpson's method, biplane) at hospital discharge were included in the study. All the patients were enrolled before the ELR application. Patients who could not be discharged from the hospital within 14 days after index MI, had comorbidities likely to limit survival to less than 12 months, had an existing pacemaker or ICD implanted, or were dialysis dependent, were excluded.

Acute MI was defined and followed as per the fourth universal definition of myocardial infarction.[6] A 7 days ELR was applied at the time of discharge (phase 1 monitoring period) and again at 8–10 weeks after the index MI (phase 2 monitoring period). The primary objective of the study was to assess the incidence of pre-defined clinically significant arrhythmias in phase 1 monitoring period. Secondary objectives included 1) assessing the incidence of clinically significant arrhythmias as recorded by ELR in phase 2 monitoring period; 2) characterizing medical interventions performed and/or indicated based on ELR findings during phases 1 and 2 monitoring periods; 3) determining if patients with non-lethal arrhythmias documented by an ELR during phases 1 and 2 monitoring periods had a higher risk of all-cause mortality at 1 year; and 4) evaluating whether there was an association between ELR reported arrhythmias and incidence of SCD, resuscitated ventricular fibrillation (VF), and appropriate ICD shock.

Clinically significant arrhythmia was predefined, by the study steering committee, based on the risk associated with arrhythmic events and medical interventions required to manage the patients. This included any episodes of VF, sustained and non-sustained ventricular tachycardia, Atrial Fibrillation, chronic atrial flutter, high degree AV block and complete heart block. Symptomatic bradycardia and tachycardia episodes and Premature Ventricular Complexes (PVC) as reported by ELR (>6 events in 45 s) were also considered as clinically significant.

Sustained VT or VF post MI is associated with high risk of mortality and an indication of ICD implantation as per guidelines.[7,8] Cardiac Arrhythmias and Risk Stratification after Acute MI (CARISMA) trial reported that any incidence of arrhythmia post MI including sinus bradycardia, AV block, AF, non-sustained VT, and sustained VT/VF is associated with reinfarction, stroke, progressive HF and death.[9] Incidence of >10 PVC's in 1 h in post MI patients is an independent risk factor of sudden death in first 6 months.[10] Ambient arrhythmias defined as > 10 PVC's/hour or NSVT was used in risk stratification of post MI patients for ICD implants in DEFINITE trial and Improve SCA study.[11,12]

A detailed list of clinically significant arrhythmias is given under supplementary Material (Annexure-1).

In this study, either the NUVANT Mobile Cardiac Telemetry ELR or SEEQ™ External Cardiac Monitor (Medtronic Inc, Minneapolis) were used to monitor arrhythmias during two periods of post MI, phases 1 and 2.[13] Each monitoring phase lasted up to 7.5 days. The ELR devices used are wireless arrhythmia detection systems that are placed on the chest to the left of the sternum, positioned diagonally from the clavicle. Once activated, the ELR continuously monitors the heart and automatically collects an electrocardiogram (ECG) when a rhythm abnormality is detected; (HR $\geq$ 130 bpm or $\leq$40 bpm, pause $\geq$3 s, frequent premature contractions (PVCs), atrial fibrillation (AF), ventricular tachycardia (VT) or Ventricular Fibrillation. Patients could also trigger an ECG when they experienced cardiac symptoms. Data were automatically transmitted wirelessly from the ELR to a bed-side hub and then to a monitoring center where certified cardiographic technicians reviewed and interpreted ECG events. Clinical reports, prepared by the monitoring center, were emailed to the prescribing physician for the diagnosis and identification of clinical conditions, events and trends. Whenever urgent events were captured by the monitoring center, reports were sent within 3 h to the physician. The ELR data were extracted for analysis from the monitoring center database.

2.1. Data collection and monitoring

At the time of enrollment, demographic information, medical history, LVEF, and information related to the index MI were collected. The ELR for phase 1 monitoring was applied before hospital discharge and patients were instructed to wear it for 7 days, after which they could remove it themselves. Follow-up visits were scheduled at 2 months, 6 months, 9 months and 12 months. At the 2-month visit after the index MI, LVEF and 12-lead ECG were collected and the phase 2 monitoring ELR was applied. Health status was checked via telephone or in-office visit at 6 and 9 months after the index MI. At 12 months, patients were seen in hospital. Telephonic health status was collected from all patients when the last patient completed the 12-month follow-up visit.

2.2. Risk scores

A predefined ELR risk score was used to assess arrhythmias detected in phase 1 monitoring period. The risk score was predefined, by the study steering committee, to assess the predictive value of arrhythmic events at acute and chronic phase of post MI for all-cause mortality at 1 year. The scores assigned to each event were: sustained polymorphic VT/VF-5; sustained monomorphic

VT-4; non–sustained polymorphic VT-3; non-sustained monomorphic VT-1 (depending on duration); PVCs (>6 in 45 s)-1; AF (≥30 s)-1; second degree AV block and complete heart block-1. Event scores where summed with a maximal value of 5. The risk scores were assigned based on relative risk of arrhythmic events and its association to incidence of mortality.[7,10–12,14–17]

Additionally, the Global Registry of Acute Coronary Events (GRACE) risk score (which was calculated from baseline data) was used as measure of overall risk.[18]

2.3. Statistical analysis

Patient characteristics are reported with mean and standard deviation, or with count and percentage. LVEF is reported with median and inter-quartile range (IQR).

The primary objective was to assess the incidence of clinically significant arrhythmias during phase 1. Patients with less than 3 days of monitoring data and no clinically significant arrhythmias detected were excluded from the analysis. Arrhythmias with onset during the first 7 days of monitoring were included and classified as clinically significant or not. The proportion of patients with any clinically significant arrhythmias is reported with the corresponding 95% confidence interval (CI) (Wilson score method).

Mortality was summarized with Kaplan–Meier estimates, and compared between patients with and without clinically significant arrhythmias with a log-rank test. Incidence of SCD, VF, or appropriate ICD shocks was analyzed similarly, using Gray's test to account for the competing risk of non-SCD death.

Cox proportional hazards regression was used to assess the independent influence of ELR monitored arrhythmias and baseline variables on mortality. Variables that were univariately significant were included in a multivariable model. The least significant variable was removed iteratively as long as the reduced model was not significantly worse at predicting mortality than the initial full multivariable model (likelihood score test).

INSPIRE-ELR was designed to include 300 patients to achieve 5% accuracy for the estimated proportion of patients with clinically significant arrhythmias.

A p-value < 0.05 was considered significant and confidence intervals are for 95% accuracy and two sided.

3. Results

The INSPIRE-ELR study enrolled 250 patients at 11 centers in India between April 2014 and January 2016. One patient was excluded due to inclusion criteria deviation. The remaining 249 patients with LVEF ≤35% at the time of discharge within 14 days following MI were predominantly male and relatively young (Table 1). Most patients had STEMI with anterior wall MI. Reperfusion had been performed in 82% of the patients and all patients were prescribed with standard of care cardiovascular medications at the time of discharge. Median LVEF was 34%, measured 5.1 ± 3.0 days after MI.

The 233 patients who completed 72 h of monitoring or had monitoring terminated because of a significant arrhythmia were included in the analysis. Sixteen patients were excluded. Out of these sixteen patients, no ELR monitoring was done ($n = 4$), did not complete 72 h ($n = 11$), or death occurred after enrollment but before monitoring could be obtained ($n = 1$). Mean monitoring duration was 7.1 ± 1.5 days. Of the 233 patients, a clinically significant arrhythmia was reported in 81 patients (34.8%, 95% CI: 28.9%–41.1%) during phase 1 monitoring period (Table 2). The most frequently reported arrhythmia was PVC (33%), followed by non-specific bradycardia (3%). Twenty-six of the 233 patients with phase 1 monitoring died during a follow-up duration of 19 ± 10 months, with 11.4% overall mortality at 12 months (CI: 7.9%–16.3%). Mortality was significantly higher in patients with clinically significant arrhythmias compared with those without (at 12 months: 23.6% vs 4.8% with 19 vs 7 deaths, HR = 5.5, 95% CI: 2.3–13.0, $p < 0.0001$) (Fig. 1A). Seven of the 26 deaths occurred during the 7 days of phase 1 monitoring and two patients were lost to follow-up. Excluding these 9 patients who have zero time at risk after acute ELR monitoring, mortality in patients with clinically significant arrhythmias remained higher than in patients without (HR = 4.5, $p < 0.001$) (Fig. 1B).

Of the163 patients who completed the phase 2 monitoring period, 61 (37.4%) had experienced clinically significant arrhythmias during the phase 2 monitoring, including VT/VF: 2 (1.2%); frequent PVCs: 54 (33.1%); AF: 3 (1.8%); 2nd or 3rd degree AV block: 1 (0.6%); and symptomatic bradycardia: 6 (3.7%). Mortality trended to be higher in patients with clinically significant arrhythmias (at 12 months after the monitoring period: 8.2% vs 2.0%, HR = 4.3 (95% CI: 0.8 to 22, $p = 0.057$) (Fig. 1C).

Clinically significant arrhythmias for which the investigator considered an intervention was indicated were detected in 5 patients (6.2%) during phase 1 and in two patients (3.3%) during phase 2. Interventions included medications for patients with AV block, sinus tachycardia, VT, AF and PVCs ($n = 5$), and ICD/CRT-D for patients with VT events ($n = 2$).

In univariable analysis, the following were significantly associated with mortality: medical history of prior myocardial infarction, AF, VF, and VT; LVEF, QRS duration, systolic blood pressure, and GRACE score at discharge; the presence of significant arrhythmia; and the ELR risk score (Table 3). In a reduced multivariable model, history of MI (HR = 2.65, 95% CI: 1.10–6.40, $p = 0.03$), QRS duration at discharge (HR = 1.20 per 10 ms, 95% CI: 1.06–1.36, $p = 0.004$), and the ELR risk score (HR = 2.01, 95% CI: 1.55–2.62, $p < 0.0001$) were independent predictors of mortality.

Association between ELR reported arrhythmias and incidence of the composite endpoint of SCD, resuscitated VF and appropriate ICD shock was assessed among 10 sudden cardiac deaths (adjudicated by an independent physician committee) and 2 VT/VF events. Patients with clinically significant arrhythmia had a higher event incidence than patients without ($p = 0.003$, Gray's test), with estimated hazard ratio HR = 6.04 (95%CI: 1.63–22.3) (Fig. 1D).

4. Discussion

The INSPIRE-ELR study conducted in acute MI patients with reduced LVEF using guideline based contemporary treatment modalities did show a high 1-year mortality (11.4%) so this group of patients are at high risk of SCD and needs different treatment strategies. In this study we were aiming at assessing if early detection of arrhythmias could be of help in predicting 1-year mortality. We were able to show a high incidence of clinically significant arrhythmias shortly after MI (phase 1 and 2 monitoring periods, at and 8–10 weeks week after hospital discharge). The presence of significant arrhythmias in the first phase was associated with 5 times higher mortality, and even with this small study we were able to show a highly significant difference in outcomes.[19]

This association was even stronger (HR = 6.04, $p = 0.003$) to the cumulative incidence of SCD and VT/VF events ($n = 12$). The ELR risk score, history of myocardial infarction and QRS duration at discharge were found to be independent predictors of mortality with a simple ELR score being the best predictor.

The VALIANT trial reported 8–9% incidence of sudden death or cardiac arrest with resuscitation at 1 year post MI in patients with LVEF ≤30%.[3] Our data included post MI patients with LVEF up to 35% and the all-cause mortality observed at 1 year was 11.4%. These numbers seem not dissimilar, but it must be noted that the

Table 1
Patient demographics and clinical characteristics.

	All patients ($n = 249$)	Analysis Cohort ($n = 233$)
Patient demographics		
Age (years)	56 ± 12	56 ± 12
Male Gender	215 (86%)	204 (88%)
Medical history		
Prior Myocardial Infarction	25 (10%)	25 (11%)
Prior CABG	3 (1%)	3 (1%)
Hypertension	52 (21%)	49 (21%)
Diabetes Mellitus	103 (41%)	96 (41%)
NYHA Class III-IV	3 (1%)	3 (1%)
History of Smoking		
Never	128 (51%)	117 (50%)
Current	54 (22%)	52 (22%)
Past	53 (21%)	50 (21%)
Index Myocardial Infarction		
STEMI	206 (83%)	192 (82%)
Anterior location	195 (78%)	182 (78%)
Reperfusion		
None	46 (18%)	41 (18%)
Time to reperfusion start (hours)	22.3 ± 41.4	23.1 ± 42.0
Thrombolysis	78 (31%)	77 (33%)
Coronary Artery Intervention	167 (67%)	158 (68%)
Angioplasty	42 (17%)	38 (16%)
Stent	152 (61%)	144 (62%)
Other	16 (6%)	16 (7%)
Characteristics at Discharge		
Height (cm)	162 ± 11	162 ± 11
Weight (kg)	65 ± 11	65 ± 12
Cardiovascular medication, any	248 (100%)	233 (100%)
Statin	230 (92%)	216 (93%)
Beta blocker	194 (78%)	182 (78%)
Antiplatelet	241 (97%)	227 (97%)
ACE Inhibitor/ARB	145 (58%)	138 (59%)
Heart Rate (bpm)	86 ± 15	86 ± 15
QRS Duration (ms)	95 ± 26	96 ± 26
Left Ventricular Ejection Fraction		
LVEF at enrollment	34 (30–35)	34 (30–35)
days after index MI	5.1 ± 3.0	5.1 ± 3.0
LVEF at Chronic monitoring	36 (34–43)	36 (35–43)
days after index MI	76 ± 15	76 ± 15

Values are n (%), mean ± standard deviation or median (inter-quartile range).
ACE, Angiotensin Converting Enzyme; ARB, Angiotensin II Receptor Blocker; CABG, Coronary Artery Bypass Grafting; LVEF, Left Ventricular Ejection Fraction; MI, Myocardial Infarction; NYHA, New York Heart Association; STEMI, ST-Elevation Myocardial Infarction.

Table 2
Incidence of arrhythmias during phase 1.

Rhythm	Patients with rhythm detected[e] N (%)	Number of arrhythmia episodes median (range)
Clinically significant		
Polymorphic VT/VF	3 (1.3%)	1 (1,2)
Monomorphic VT	8 (3.4%)	1 (1–6)
Non-Sustained Ventricular Tachycardia	0 (0.0%)	
Premature Ventricular Complexes (PVC)[a]	65 (27.9%)	2 (1–53)
Atrial Fibrillation (AF)[b]	8 (3.4%)	3 (1–8)
Chronic Atrial Flutter	4 (1.7%)	3 (1–4)
Non-specific Supra-Ventricular Tachycardia[c]	1 (0.4%)	1 (1–1)
Sinus Tachycardia[c]	1 (0.4%)	1 (1–1)
Sinus Bradycardia[c]	2 (0.9%)	6 (3–8)
Bradycardia (nonspecific)[c]	6 (2.6%)	1 (1–11)
Mobitz 1[c]	0 (0.0%)	
Mobitz 2	0 (0.0%)	
High degree heart block	2 (0.9%)	3 (1–5)
Complete heart block	2 (0.9%)	2 (1,2)
Pause[d]	0 (0.0%)	

AF, Atrial Fibrillation; ELR, External Loop Recorder; PVC, Premature Ventricular Contraction; VT, Ventricular Tachycardia; VF, Ventricular Fibrillation.
[a] Greater than 6 per 45 s (ELR detection criteria).
[b] Any episode lasting more than 30 s.
[c] Symptomatic episodes.
[d] Recurrent symptomatic episodes.
[e] Number and percentage of patients experiencing the arrhythmia in the first 7 days of ELR application.

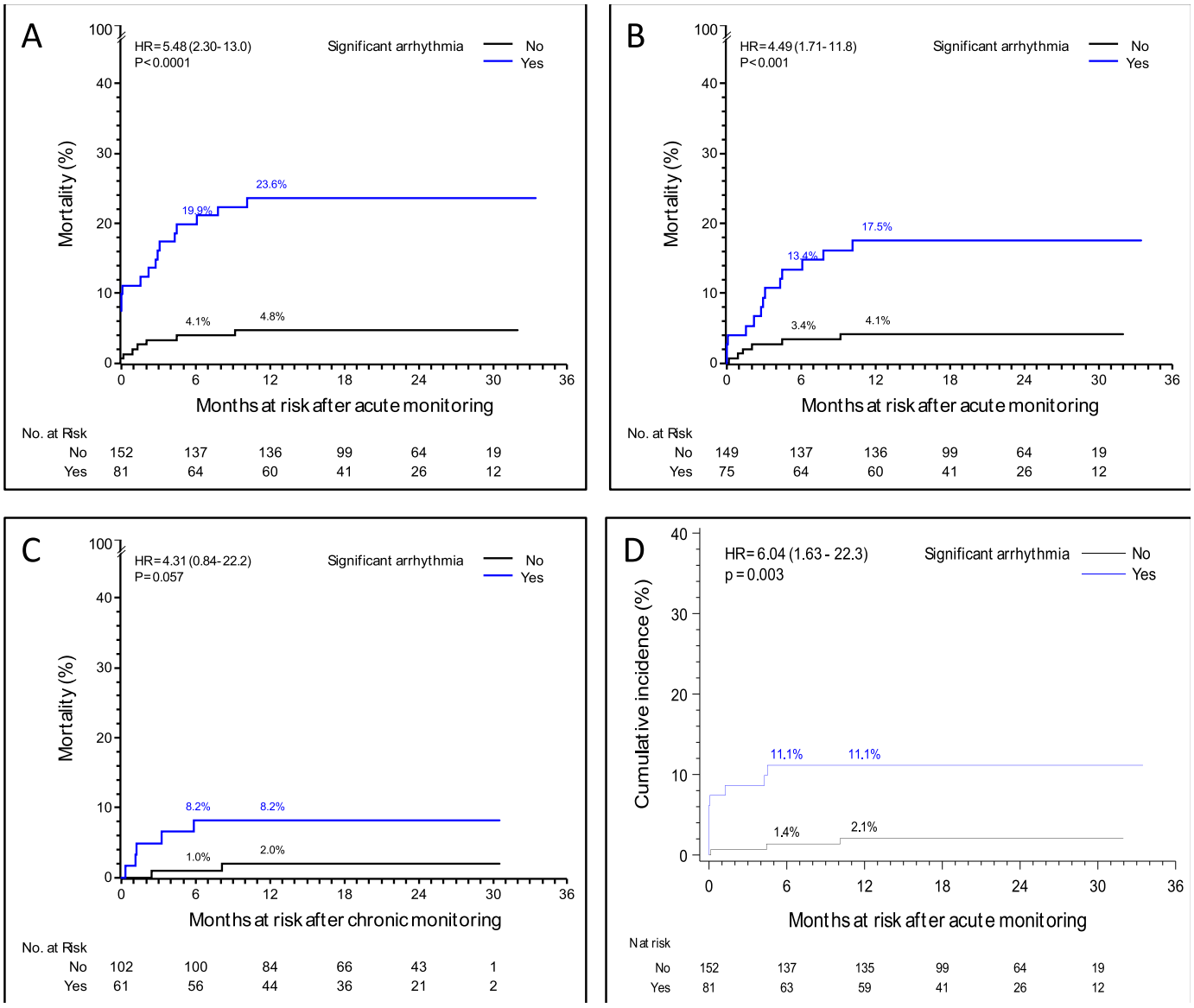

Fig. 1. (A) Mortality in relation to acute arrhythmia monitoring. (B) Mortality in relation to arrhythmias during acute monitoring excluding early deaths (C) Mortality in relation to chronic arrhythmia monitoring (D) Association between ELR reported arrhythmias and composite of incidence of SCD, resuscitated ventricular fibrillation and appropriate ICD shock.

VALIANT data is more than 10 years older than our data. On the other hand, the time to reperfusion of 22.3 ± 41.4 h is relatively long and may have contributed to a relatively high mortality.

Post MI arrhythmias recorded by ELR during phase 1 monitoring period were dominated by PVCs (33% patients), followed by non-specific Bradycardia (3%). Previous studies have reported frequent incidence of PVCs in acute MI patients and its association with SCD[10,20,21] however these are old data. Frequent PVCs documented >40 days post MI have been suggested to identify high risk patients for primary prevention ICD implantation.[22] But there have been no recommendations for these arrhythmias in the first month after MI.

There is currently no conclusive evidence available on the effectiveness of drug or defibrillator implantation for preventing death in patients with acute MI. Even though ICDs significantly reduced arrhythmic deaths in both the IRIS and DINAMIT studies, this was counterbalanced by a higher number of deaths from non-arrhythmic cardiac causes.[4,23] The reasons for the negative results of these studies were widely discussed. The heart rate variability measure used for risk stratification in DINAMIT was shown to be more associated with all-cause mortality than SCD.[24] Less than 5% of post MI patients meet IRIS study criteria, which questions how representative the study cohort in this study was of the general post MI population. We cannot say from this study if we could alter the mortality rates by implanting ICDs in these patients since this was not the aim of present study. Even the recent VEST trial on wearable Cardioverter–Defibrillator after Myocardial Infarction with LVEF<35% did not show benefit by lowering the arrhythmic death.[25] We hypothesize that wearable defibrillator or ICD implant in only high-risk patients with low LVEF (LVEF <35%) early after MI may be of benefit.

Differences in patient profile and practice patterns compared to developed countries were observed. Patients in the INSPIRE-ELR study conducted in India were relatively younger (56 ± 12 yrs), predominantly male (86%), with STEMI (83%), anterior wall MI (78%), and a diabetes background (41%). This age and gender

Table 3
Predictive value of ELR risk score and baseline variables for mortality.

Variable	Univariable Hazard Ratio (CI) *p*-value	Multivariable Hazard Ratio (CI) *p*-value	Reduced multivariable Hazard Ratio (CI) *p*-value
Demographics			
Age at enrollment[b]	1.20 (0.87–1.65) p = 0.26		
Gender	0.90 (0.27–2.99) p = 0.86		
Medical History			
Prior MI	3.20 (1.35–7.63) p = 0.008	2.55 (0.92–7.08) p = 0.073	2.45 (0.99–6.07) p = 0.053
Congestive Heart Failure	3.67 (0.50–27.12) p = 0.20		
Atrial Fibrillation	9.40 (2.20–40.09) p = 0.002	0.88 (0.10–7.42) p = 0.91	
Ventricular Fibrillation	6.49 (2.23–18.90) p < 0.001	1.27 (0.14–11.18) p = 0.83	
Ventricular Tachycardia	7.61 (1.79–32.33) p = 0.006	0.20 (0.01–3.46) p = 0.27	
Diabetes	1.51 (0.70–3.26) p = 0.29		
MI characteristics			
Positive initial enzymes	1.47 (0.62–3.50) p = 0.38		
STEMI	1.08 (0.41–2.86) p = 0.88		
Anterior wall infarct	0.62 (0.27–1.43) p = 0.27		
Reperfusion done	0.83 (0.33–2.07) p = 0.69		
Reperfusion <3 h in STEMI	N.A.[a] p = 0.99		
Coronary Artery Intervention	0.88 (0.39–1.98) p = 0.77		
Discharge assessments			
LVEF[b]	0.32 (0.14–0.72) p = 0.006	0.99 (0.31–3.11) p = 0.98	
Heart rate[b]	1.15 (0.90–1.47) p = 0.25		
QRS duration[b]	1.21 (1.08–1.35) p = 0.001	1.23 (1.06–1.41) p = 0.005	1.18 (1.04–1.34) p = 0.010
Systolic Blood Pressure[b]	0.78 (0.63–0.97) p = 0.024	0.84 (0.65–1.09) p = 0.19	
GRACE score	1.70 (1.08–2.69) p = 0.023	1.42 (0.80–2.55) p = 0.23	
Discharge medication			
ACE inhibitor	1.02 (0.47–2.20) p = 0.96		
ARB	N.A.[a] p = 0.99		
Antiplatelet	0.57 (0.08–4.24) p = 0.59		
Beta blocker	0.52 (0.23–1.17) p = 0.11		
Diuretic	2.22 (1.01–4.88) p = 0.048	0.82 (0.32–2.11) p = 0.68	
Anticoagulant	3.85 (0.91–16.29) p = 0.067		
Statin	0.61 (0.18–2.03) p = 0.42		
Cardiac glycoside	2.15 (0.87–5.37) p = 0.099		
Vasodilator or nitrate	1.15 (0.51–2.57) p = 0.74		
Antiarrhythmic	9.60 (3.59–25.72) p < 0.0001	5.55 (0.77–40.03) p = 0.089	2.41 (0.75–7.74) p = 0.14
ELR assessments			
Significant Arrhythmia on ELR	5.48 (2.30–13.04) p < 0.001	1.77 (0.49–6.34) p = 0.38	
PVC's on ELR[c]	2.24 (1.03–4.83) p = 0.041		
ELR risk score	1.93 (1.52–2.45) p < 0.0001	1.70 (1.08–2.67) p = 0.022	1.83 (1.36–2.46) p < 0.0001

ACE, Angiotensin Converting Enzyme; ARB, Angiotensin II Receptor Blocker; CI, Confidence Interval; ELR, External Loop Recorder; GRACE, Global Registry of Acute Coronary Events; LVEF, Left Ventricular Ejection Fraction; MI, Myocardial Infarction; PVC, Premature Ventricular Contraction; STEMI, ST-Elevation Myocardial Infarction.
[a] Relation cannot be determined.
[b] Hazard ratio per 10 units.
[c] Not considered in multivariable model.

distribution is in line with other studies conducted on patients with Acute Coronary Syndrome (ACS) in this country.[26,27]

The results from the Global Registry of Acute Coronary Events (GRACE) show that patients were on average a decade older, fewer presented with STEMI (40%) and there was a shorter time to intervention after MI.[18,28,29] The CARISMA trial conducted in Europe also reported higher average age (65 + 11 years) compared to this study.[9]

The majority of patients underwent reperfusion therapy comparable to the contemporary practices and patients received standard of care medical management at discharge. However, time between MI and arrival in hospital was long compared to contemporary Western standards.

The evidence from the present study show that ELRs can be used to risk stratify patients early after MI. A prospective study is needed to evaluate whether ventricular arrhythmia is a major contributor to all-cause mortality and if early implantation of ICDs can be beneficial to manage these high-risk patients.

4.1. Limitations

The study enrolled only 250 patients of the planned 300. Consequently, the confidence interval for percentage of patients with clinically significant arrhythmia was wider than postulated per study design (12.2% vs 10.0%), also due to the higher than expected proportion of patients with arrhythmias (34.8% vs 25%).

5. Conclusions

The INSPIRE-ELR study showed that there is high incidence of clinically significant arrhythmia early after MI detected by External Loop Recorder (ELR). ELR applied in patients with acute MI and LV dysfunction at the time of discharge identifies patients with high mortality risk.

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Declaration of competing interest

V. Rajan and B. Gerritse are employees of Medtronic. None of the other authors has any disclosures.

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Appendix A. Supplementary data

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References

1. Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation*. 2015;132:1667–1678.
2. Adabag AS, Therneau TM, Gersh BJ, Weston SA, Roger VL. Sudden death after myocardial infarction. *JAMA*. 2008;300:2022–2029.
3. Solomon SD, Zelenkofske S, McMurray JJV, et al. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *N Engl J Med*. 2005;352:2581–2588.
4. Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter–defibrillator after acute myocardial infarction. *N Engl J Med*. 2004;351:2481–2488.
5. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American college of cardiology/American heart association task force on practice guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices). *J Am Coll Cardiol*. 2008;51:e1–e62.
6. Thygesen K, Alpert JS, Jaffe AS, et al. The executive group on behalf of the joint European society of cardiology (ESC)/American college of cardiology (ACC)/American heart association (AHA)/World heart Federation (WHF) task force for the universal definition of myocardial infarction. Fourth universal definition of myocardial infarction (2018). *Circulation*. 2018;138:e618–e651.
7. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med*. 1996;335:1933–1940. JID - 0255562.
8. Priori SG, Blomström-Lundqvist C, Mazzanti A, et al. ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC). Endorsed by: association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J*. 2015;36:2793–2867. https://doi.org/10.1093/eurheartj/ehv316, 2015.
9. Bloch Thomsen PE, Jons C, Raatikainen MJ, et al. Long-term recording of cardiac arrhythmias with an implantable cardiac monitor in patients with reduced ejection fraction after acute myocardial infarction: the Cardiac Arrhythmias and Risk Stratification after Acute Myocardial Infarction (CARISMA) study. *Circulation*. 2010;122:1258–1264.
10. Maggioni AP, Zuanetti G, Franzosi MG, et al. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era. GISSI-2 results. *Circulation*. 1993;87:312–322.
11. Kadish A, Dyer A, Daubert JP, et al. Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) Investigators. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med*. 2004 May 20;350(21):2151–2158. https://doi.org/10.1056/NEJMoa033088. PMID: 15152060.
12. Zhang, et al. Utilization of implantable cardioverter-defibrillators for the prevention of sudden cardiac death in emerging countries: Improve SCA clinical trial. *Heart Rhythm*. 2020 Mar;17(3):468–475. https://doi.org/10.1016/j.hrthm.2019.09.023.
13. Shrivastav M, Padte S, Arora V, Biffi M. Pilot evaluation of an integrated monitor-adhesive patch for long-term cardiac arrhythmia detection in India. *Expert Rev Cardiovasc Ther*. 2014 Jan;12(1):25–35. https://doi.org/10.1586/14779072.2013.867807. Epub 2013 Dec 10. PMID: 24325206.
14. Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med*. 1997 Nov 27;337(22):1576–1583. https://doi.org/10.1056/NEJM199711273372202. PMID: 9411221.
15. Connolly SJ, Gent M, Roberts RS, et al. Canadian implantable defibrillator study (CIDS) : a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation*. 2000 Mar 21;101(11):1297–1302. https://doi.org/10.1161/01.cir.101.11.1297. PMID: 10725290.
16. de Sousa MR, Morillo CA, Rabelo FT, Nogueira Filho AM, Ribeiro AL. Non-sustained ventricular tachycardia as a predictor of sudden cardiac death in patients with left ventricular dysfunction: a meta-analysis. *Eur J Heart Fail*. 2008 Oct;10(10):1007–1014. https://doi.org/10.1016/j.ejheart.2008.07.002. Epub 2008 Aug 9. PMID: 18692437.
17. Verma A, Sarak B, Kaplan AJ, et al. Predictors of appropriate implantable cardioverter defibrillator (ICD) therapy in primary prevention patients with ischemic and nonischemic cardiomyopathy. *Pacing Clin Electrophysiol*. 2010 Mar;33(3):320–329. https://doi.org/10.1111/j.1540-8159.2009.02566.x. Epub 2009 Oct 1. PMID: 19796352.
18. Fox KAA, Goodman SG, Klein W, et al. Management of acute coronary syndromes. Variations in practice and outcome: findings from the global registry of acute coronary events (GRACE). *Eur Heart J*. 2002;23:1177–1189.
19. Singh B, Rao H, Pandurangi U, et al. Identifying high-risk patients post myocardial infarction with reduced left ventricular function using external loop recorders (INSPIRE-ELR study). *J Am Coll Cardiol*. 2018;71:A432.
20. Ruberman W, Weinblatt E, Goldberg JD, Frank CW, Chaudhary BS, Shapiro S. Ventricular premature complexes and sudden death after myocardial infarction. *Circulation*. 1981;64:297–305.
21. Bigger JT. Relation between left ventricular dysfunction and ventricular arrhythmias after myocardial infarction. *Am J Cardiol*. 1986;57:8B–14B.
22. Zhang S, Singh B, Rodriguez DA, et al. Improve the prevention of sudden cardiac arrest in emerging countries: the Improve SCA clinical study design. *Europace*. 2015;17:1720–1726.
23. Steinbeck G, Andresen D, Seidl K, et al. Defibrillator implantation early after myocardial infarction. *N Engl J Med*. 2009;361:1427–1436.
24. Bilchick KC, Fetics B, Djoukeng R, et al. Prognostic value of heart rate variability in chronic congestive heart failure (veterans affairs' survival trial of antiarrhythmic therapy in congestive heart failure). *Am J Cardiol*. 2002;90:24–28.
25. Olgin JE, Pletcher MJ, Vittinghoff E, et al. Wearable cardioverter–defibrillator after myocardial infarction. *N Engl J Med*. 2018;379:1205–1215.
26. Rao BH, Sastry BKS, Korabathina R, et al. Sudden cardiac death after acute ST elevation myocardial infarction: insight from a developing country. *Heart Asia*. 2012;4:83e89.
27. Xavier D, Pais P, Devereaux PJ, et al. For the CREATE Registry Investigators. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*. 2008;371:1435–1442.
28. Budaj A, Brieger D, Steg PG, et al. Global patterns of use of antithrombotic and antiplatelet therapies in patients with acute coronary syndromes: insights from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J*. 2003;146:999–1006.
29. Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol*. 2002;90:358–363.