Circumstances and Outcomes of Sudden Unexpected Death in Patients With High-Risk Myocardial Infarction

Implications for Prevention

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Background—Sudden death (SD) is a frequent catastrophic complication in patients after myocardial infarction. Circumstances of SD may affect strategies for prevention.

Methods and Results—We reviewed source documentation for 1067 patients who had SD in the Valsartan in Acute Myocardial Infarction Trial (VALIANT) trial. We determined the circumstances of these events and assessed long-term mortality in patients who were resuscitated. Location of the SD event was available in 978 of 1067 patients, with 226 events occurring within the first 40 days. Although SD was more likely to occur at home (645 of 978, 66%) than in hospital (204 of 978, 21%), the proportion of in-hospital events was higher early on (99 of 226, 44%). Home events were less likely to be witnessed regardless of time frame. Preceding activity was known for 42% of patients with home arrest; of these, 52% were determined to be asleep at time of event, and these deaths were more likely to be unwitnessed. A majority of patients for whom initial ECG rhythm was reported had ventricular tachycardia/ventricular fibrillation (189 of 283, 67%). Of the 155 patients successfully resuscitated, 24% subsequently received an implantable cardioverter-defibrillator. Nineteen percent of those who received an implantable cardioverter-defibrillator subsequently died compared with 49% of patients who did not receive an implantable cardioverter-defibrillator (hazard ratio, 0.36; 95% confidence interval, 0.14 to 0.93; $P=0.04$).

Conclusions—A high proportion of SD events after high-risk myocardial infarction occurred at home, but in-hospital events were more common early on. Patients who were asleep were more likely to have unwitnessed arrests. Alternative strategies for the prevention of SD in patients who are not candidates for implantable cardioverter-defibrillator will need to take into account the circumstances of SD events. **(*Circulation*. 2011;123:2674-2680.)**

Key Words: arrhythmia, cardiac ■ death, sudden ■ defibrillators, implantable ■ myocardial infarction ■ tachycardia, ventricular

The risk of sudden unexpected death is elevated in survivors of acute myocardial infarction (MI).[1–4] Although primary prevention with implantable cardioverter-defibrillators (ICDs) is of known benefit in a select subset of high-risk patients with reduced left ventricular ejection fraction, strategies for preventing sudden death in those who are not eligible for ICD therapy remain elusive.[5–7] In particular, both the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) and the Immediate Risk-Stratification Improves Survival (IRIS) trial failed to demonstrate any mortality benefit for early ICD implantation in post-MI patients with decreased ejection fraction,[8,9] despite the substantial burden of sudden death events in this population.[3] In part to address this therapeutic lack, the Home Automated External Defibrillator Trial (HAT) investigated the use of home automated external defibrillators (AEDs) in patients with history of anterior MI who were otherwise not candidates for ICD.[10] Despite a small number of patients who were successfully resuscitated with home AEDs, the trial failed to demonstrate significant improvement in overall survival. A high proportion of unwitnessed home arrests may have contributed to the lack of a statistical benefit because AEDs require bystanders to be present to operate the device and to achieve successful defibrillation.[7,11]

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Clinical Perspective on p 2680

Although the circumstances of out-of-hospital cardiac arrest in the general population have been well described, there has been only limited characterization of the context of sudden death events in patients with prior MI.[12–16] To better understand the circumstances and outcomes of sudden death events over time in high-risk patients after MI, we studied patients with sudden unexpected death or cardiac arrest with resuscitation in the Valsartan in Acute Myocardial Infarction Trial (VALIANT).

Methods

The double-blind, randomized, controlled VALIANT assessed treatment with valsartan, captopril, or both in 14 703 patients with acute MI complicated by heart failure, left ventricular systolic dysfunction, or both.[17] Patients were enrolled at 931 hospitals in 24 countries between December 1998 and June 2001. For this analysis, 94 patients who received an ICD before randomization were excluded. A detailed description of the population and protocol, including inclusion and exclusion criteria, has been published previously.[12]

A central, blinded adjudication committee reviewed all deaths and episodes of cardiac arrest with resuscitation using source documentation provided by individual sites. Sudden death was explicitly defined as death that occurred suddenly and unexpectedly in a patient who was otherwise clinically stable, with no documentation of heart failure, MI, or another clear cause of death; except for rare cases, deaths during the index hospitalization were not adjudicated as sudden death. Sudden death events were further adjudicated by the central committee into 3 categories: witnessed, not witnessed, but with the patient seen within 1 hour of death, and not witnessed, with the patient seen >1 hour but <24 hours before death. Patients who were last seen >24 hours before death were not considered to have had sudden death. The time course of sudden cardiac death in VALIANT has been previously described.[3] Cardiac arrest with resuscitation was defined as cardiac arrest from which the patient regained consciousness and subsequent cognitive function, even if briefly. For the purposes of this analysis, cardiac arrests with resuscitation were categorized as witnessed events.

Source documentation for all episodes of sudden unexpected deaths or cardiac arrest with resuscitation was reviewed when available. A standardized abstraction instrument was used to capture data elements pertaining to circumstances of the arrest event, including location of event, preceding symptoms, preceding activity, and initial ECG rhythm, if known. Location was classified as at home, in hospital (including emergency room), or at other public settings. The presence of preceding symptoms was defined as symptoms within 24 hours of the event that could be retrospectively interpreted as being of cardiac origin, including chest discomfort, dyspnea, syncope, or other.[18] For preceding activity, each patient was classified as being asleep at the time of sudden death if there was witnessed account of patient sleeping, or, for arrests that were not witnessed, if the patient was found recumbent in bed. Initial ECG rhythm was defined as the initial rhythm documented after the arrest had taken place. For patients who were classified as being awake, whether the patient was physically active or at rest at the time of event was also recorded. In addition, we described in detail the above measures for patients who experienced sudden death events within first 40 days and first 90 days of their index MI.

For patients who experienced cardiac arrest with resuscitation, we identified those who received ICD implantation within 42 days of the event and those who did not. All comparisons of baseline clinical characteristics were performed with the Student t test for continuous variables and the χ^2 test for categorical variables. To account for potential survivor bias, we performed a landmark analysis using Kaplan–Meier methods by excluding patients who died or were censored within 42 days of their initial event. Hazard ratios were derived through the use of step-wise Cox proportional hazards regression with a cutoff of $P<0.05$ for all baseline covariates that had value of $P\leq 0.20$ in the initial univariate analysis, as per Maldonado and Greenland.[19] Assumption of proportional hazards for each covariates and globally was confirmed with a formal significance test based on Schoenfeld residuals. All statistical analysis was performed with STATA version 10.0 (Stata Corp, College Station, TX).

Results

Of 14 609 patients enrolled in VALIANT who were eligible for analysis, 1067 (7%) had sudden death or cardiac arrest, including 903 patients who died and 164 patients who were resuscitated after cardiac arrest. In total, 1486 patients died of nonsudden cardiovascular causes and 385 patients of noncardiovascular causes. Compared with surviving patients without events, patients who had sudden unexpected death or cardiac arrest with resuscitation were significantly older; had higher baseline systolic and diastolic blood pressures and high baseline heart rate; had higher Killip class and lower left ventricular ejection fraction; had higher rates of diabetes mellitus, hypertension, and prior MI; were less likely to have been treated with percutaneous coronary intervention or thrombolytic therapy; and were less likely to have been receiving β-blockers or amiodarone (Table 1). As our group has reported previously,[3] baseline characteristics between patients who died of other causes, both cardiovascular and noncardiovascular, and patients who had sudden unexpected death or cardiac arrest resuscitation, were much more similar.

Source documentation was available for 1062 of 1067 patients who had sudden death or cardiac arrest. Of these, 251 patients had an event within the first 40 days of their index MI, 140 patients had an event 41 to 90 days after their index MI, and 671 patients had an event >90 days after their index MI. The presence or absence of preceding symptoms was documented for 710 of 1062 patients (Table 2). A majority of patients did not have any preceding symptoms (385 of 710, 54%). Of the 325 patients (46%) for whom preceding symptoms were reported, shortness of breath (165 of 325, 51%) and chest pain (161 of 325, 50%) were the most common. Initial ECG rhythm was reported for 283 of 1062 patients (Table 2), of which two thirds were ventricular fibrillation or ventricular tachycardia (189 of 283, 67%), followed by asystole (59 of 283, 21%) and pulseless electric activity (17 of 283, 6%). Compared with the entire cohort, patients who had events within the first 40 days of their index MI had essentially identical preceding symptoms and initial ECG rhythms (Table 2), as did patients who had events within the other specified time periods.

The location at which sudden unexpected death or cardiac arrest resuscitation occurred was documented for 978 of 1062 patients. Roughly two thirds of sudden death events happened at home (645 of 978, 66%) compared with approximately one fifth of events that occurred in hospital (204 of 978, 21%); the remainder of events took place in settings that were outside the home, but not in hospital (129 of 978, 13%). However, the proportion of events that occurred in hospital was higher for patients who had sudden death within the first 40 days (99 of 226, 44%) of their index MI, which then diminished over time. Only a small proportion of events occurring >90 days after index MI took place in hospital (83 of 623, 13%). Regardless of the time frame, only about half of the sudden death events that occurred at home were witnessed compared

Table 1. Baseline Characteristics of Patients According to Study Outcome

Characteristic	Sudden Unexpected Death or Cardiac Arrest With Resuscitation (n=1067)	Death Resulting From Nonsudden Cardiovascular Causes (n=1486)	Death Resulting From Noncardiovascular Causes (n=385)	Survival Free of Sudden Death or Cardiac Arrest With Resuscitation (n=11 671)
Age, y	67.8±11.2	71.2±10.3*	71.7±10.3*	63.5±11.7*
Male, %	67	60*	66	70*
Blood pressure, mm Hg				
Systolic	125.1±18.2	123.3±17.3*	123.9±17.8	122.3±16.7*
Diastolic	73.3±12.0	72.1±11.9*	71.5±11.8*	72.3±11.1*
Heart rate, bpm	78.1±13.6	79.7±13.9*	76.7±13.0	75.6±12.5*
Body mass index, kg/m^2	27.7±5.7	27.3±5.0*	26.5±5.2*	28.0±5.3*
Killip class, %				
I	20	16*	22	30*
II	46	46	49	49
III	26	28	21	15
IV	9	11	8	5
Clinical or radiographic evidence of CHF, %	83	86*	82	75*
Prior MI, %	45	42	37*	24*
Diabetes mellitus, %	31	33	27	21*
Hypertension, %	64	65	59	53*
β-blocker, %	61	56*	64	73*
Amiodarone, %	4	5	5	8*
Primary PCI, %	8	8	9	17*
Thrombolytic therapy, %	24	25	26	38*
Primary PCI or thrombolytic therapy, %	30	31	34	50*
LVEF, %	32.1±10.0	32.6±10.2	34.1±10.5*	36.0±10.3*

CHF indicates heart congestive heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; and LVEF, left ventricular ejection fraction. Values are mean±SD when appropriate. Percentages may not sum to 100 because of rounding.

*Denotes $P<0.05$ vs sudden unexpected death or cardiac arrest with resuscitation.

with the much higher proportion of witnessed events that occurred in hospital and in other public settings (Table 2).

We assessed preceding activity for the 645 patients who had sudden unexpected death or cardiac arrest with resuscitation at home. Preceding activity was known for 269 of 645 patients (42%; Table 3). Of these, half were determined to have been asleep at the time of event (139 of 269, 52%), and the remainder were determined to have been awake (130 of 269, 48%). The patients who were determined to be asleep at the time of arrest were far less likely to have witnessed events (27 of 139, 19%) compared with those who were determined to be awake (91 of 130; 70%). For patients who were determined to be awake, a third were reported to have been physically active at the time of the event (48 of 130, 37%), whereas half were reported to have been at rest (65 of 130; 50%). A similar proportion of patients with sudden death events who were determined to be asleep versus awake was observed during all time periods, with similar rates of witnessed events (Table 3).

Outcomes of Resuscitated Patients

Of the 1067 patients who had sudden death or cardiac arrest, 164 were successfully resuscitated. Compared with those in whom resuscitation was not successful, patients who were resuscitated were more likely to have had an event in hospital, to have been randomized in the United States, and to have been treated with thrombolytic therapy or percutaneous coronary intervention during their index MI. Other clinical and demographic covariates were not significantly different between the 2 groups. Of the 164 patients who had cardiac arrest with resuscitation, 4 had ICD implantation before the event. Another 5 patients died on the same day despite initial successful resuscitation. Of the 155 remaining patients, 37 (24%) subsequently received ICD implantation within 42 days of the sudden death event. The median time between sudden death event and ICD implantation was 11 days. Compared with the 118 patients who had cardiac arrest with resuscitation but did not undergo ICD implantation, those who received an ICD were significantly more likely to be male, to have higher peak creatine kinase at the time of the index MI, to have undergone primary percutaneous coronary intervention at the time of the index MI, and to have been randomized in the United States (Table 4). Other covariates, including age, body mass index, estimated glomerular filtration rate, history of MI or heart failure, time from index MI to cardiac arrest with resuscitation, and proportion of cardiac

Table 2. Details of Sudden Death Events

	Total (n=1062), n (%)	Within 40 Days of Index MI (n=251), n (%)	41 to 90 Days After Index MI (n=140), n (%)	>90 Days After Index MI (n=671), n (%)
Symptoms				
Preceding symptoms present*	325 (31)	80 (32)	36 (26)	209 (31)
Shortness of breath	165/325 (51)	42/80 (52)	16/36 (44)	107/209 (51)
Chest pain	161/325 (50)	44/80 (55)	17/36 (47)	100/209 (48)
Syncope	35/325 (11)	9/80 (11)	4/36 (11)	22/209 (11)
Other	76/325 (23)	14/80 (18)	6/36 (17)	56/209 (27)
No preceding symptoms	385 (36)	85 (34)	52 (37)	248 (37)
Unknown symptoms	352 (33)	86 (34)	52 (37)	214 (32)
Initial ECG rhythms				
Initial rhythm recorded	283 (27)	114 (45)	33 (24)	136 (20)
VF/VT	189/283 (67)	80/114 (70)	22/33 (67)	87/136 (64)
Asystole	59/283 (21)	22/114 (19)	7/33 (21)	30/136 (22)
PEA	17/283 (6)	5/114 (4)	3/33 (9)	9/136 (7)
Other	18/283 (6)	7/114 (6)	1/33 (3)	10/136 (7)
Unknown rhythm	779 (73)	137 (55)	107 (76)	535 (80)
Location of arrest				
Location known	978 (92)	226 (90)	129 (92)	623 (93)
Home	645/978 (66)	117/226 (52)	96/129 (74)	432/623 (69)
Witnessed	320/645 (50)	62/117 (53)	52/96 (54)	206/432 (48)
Unwitnessed	325/645 (50)	55/117 (47)	44/96 (46)	226/432 (52)
Hospital	204/978 (21)	99/226 (44)	22/129 (17)	83/623 (13)
Witnessed	179/204 (88)	90/99 (91)	19/22 (86)	70/83 (84)
Unwitnessed	25/204 (12)	9/99 (9)	3/22 (14)	13/83 (16)
Other public setting	129/978 (13)	10/226 (4)	11/129 (9)	108/623 (17)
Witnessed	97/129 (75)	9/10 (90)	6/11 (55)	82/108 (76)
Unwitnessed	32/129 (25)	1/10 (10)	5/11 (45)	26/108 (24)
Location unknown	84 (8)	25 (10)	11 (8)	48 (7)

VF indicates ventricular fibrillation; VT, ventricular tachycardia; and PEA, pulseless electric activity. Percentages may not add up to 100% because of rounding.

*More than 1 preceding symptoms may be reported for each patient.

arrest with resuscitation occurring within 40 days of index MI, were similar between the 2 groups. The mean and median durations of follow-up were 474.9 and 451 days, respectively.

Of the 37 patients who received an ICD, 7 (19%) subsequently died during the follow-up period compared with 58 of 118 patients (49%) who did not receive an ICD. To account for potential survivor bias, we excluded all patients who died or were censored within 42 days of their initial event from further analysis, including 25 who did not receive an ICD and 3 who did. We then applied stepwise variable selection using

Table 3. Preceding Activity and Witness Status for Patients Who Had Sudden Unexpected Death or Cardiac Arrest With Resuscitation at Home*

	Sudden Death at Home, Total (n=645), n (%)	Within 40 Days of Index MI (n=117), n (%)	41 to 90 Days After Index MI (n=96), n (%)	>90 Days After Index MI (n=432), n (%)
Preceding activity known	269 (42)	40 (34)	39 (41)	190 (44)
Determined to be awake	130/269 (48)	18/40 (45)	17/39 (44)	95/190 (50)
Witnessed event	91/130 (70)	15/18 (83)	12/17 (71)	64/95 (67)
Last seen within 1 h of discovery	23/130 (18)	1/18 (6)	3/17 (18)	19/95 (20)
Last seen >1 h before discovery	16/130 (12)	2/18 (11)	2/17 (12)	12/95 (13)
Determined to be asleep	139/269 (52)	22/40 (55)	22/39 (56)	95/190 (50)
Witnessed event	27/139 (19)	3/22 (14)	6/22 (27)	18/95 (19)
Last seen within 1 h of discovery	17/139 (12)	0/22 (0)	4/22 (18)	13/95 (14)
Last seen >1 h before discovery	95/139 (69)	19/22 (86)	12/22 (55)	64/95 (67)
Preceding activity unknown	376 (58)	77 (66)	57 (59)	242 (56)

MI indicates myocardial infarction. Percentages may not add up to 100% because of rounding.

Table 4. Baseline Characteristics of Patients With Cardiac Arrest With Resuscitation by Subsequent Implantation of a Cardioverter-Defibrillator

Characteristics	Cardiac Arrest With Resuscitation Without ICD	Cardiac Arrest With Resuscitation With ICD	*P*
Patients, n	118	37	
Age at time of index MI, y	67.5±10.3	65.1±9.8	0.20
Male sex, n (%)	79 (67)	31 (84)	0.049
Systolic blood pressure, mm Hg	120 (110–130)	118 (110–130)	0.57
Body mass index, kg/m^2	27.7±5.5	29.0±4.7	0.21
eGFR, mL · min^{-1} · 1.73 m^{-2}	64.7±22.0	67.5±20.5	0.49
LVEF, %	31.1±8.0	31.1±8.8	0.98
Previous MI, n (%)	54 (46)	14 (38)	0.40
Previous heart failure, n (%)	28 (24)	8 (22)	0.79
Diabetes mellitus, n (%)	30 (25)	13 (35)	0.25
Peak CK at time of index MI, U/L	856 (466–2237)	1994 (577–3466)	0.011
Primary PCI at time of index MI, n (%)	40 (34)	23 (62)	0.0003
Time from index MI to cardiac arrest with resuscitation, d	158.9±21.4	205.8±50.2	0.33
Cardiac arrest with resuscitation within first 40 d of index MI, n (%)	59 (50)	16 (43)	0.47
Randomized in United States, n (%)	20 (17)	24 (65)	<0.0001

ICD indicates implantable cardioverter-defibrillator; MI, myocardial infarction; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; CK, creatine kinase; and PCI, percutaneous coronary intervention.

all covariates with a value of $P \leq 0.20$ in the univariate analysis, including age at time of index MI, sex, peak creatine kinase, primary percutaneous coronary intervention, and randomization in the United States. The only covariates that remained in the model and were significant were ICD placement (hazard ratio, 0.36; 95% confidence interval, 0.14 to 0.93; $P=0.04$; the Figure) and age (hazard ratio, 1.04 for each year of increasing age; 95% confidence interval, 1.01 to 1.07; $P=0.01$). The hazard ratio for ICD placement was similar to that in the unadjusted model (hazard ratio, 0.35; 95% confidence interval 0.13 to 0.89; $P=0.03$). The assumptions of proportional hazards for both models were confirmed for each covariate and globally with a formal significance test based on Schoenfeld residuals. Finally, restricting the analysis to those who had cardiac arrest with resuscitation within first 40 days of the index MI changed the hazard ratio slightly, but the *P* value was no longer significant (hazard ratio, 0.44; 95% confidence interval, 0.10 to 2.01; $P=0.29$).

Discussion

In this retrospective analysis of patients enrolled in VALIANT, we described the circumstances and outcomes of sudden unexpected death and cardiac arrest with resuscitation in survivors of acute MI with left ventricular dysfunction, heart failure, or both. We showed that sudden death events were often heralded by preceding symptoms, and the initial ECG rhythms were often ventricular tachycardia or ventricular fibrillation. Overall, the most frequent location for sudden death events was home, although early after MI, a higher proportion of events occurred in hospital. Regardless of the time frame, events at home were less likely to be witnessed, especially if the onset was during sleep. For patients who had cardiac arrest with resuscitation, those who subsequently received ICD implantation appeared to have a much more favorable outcome.

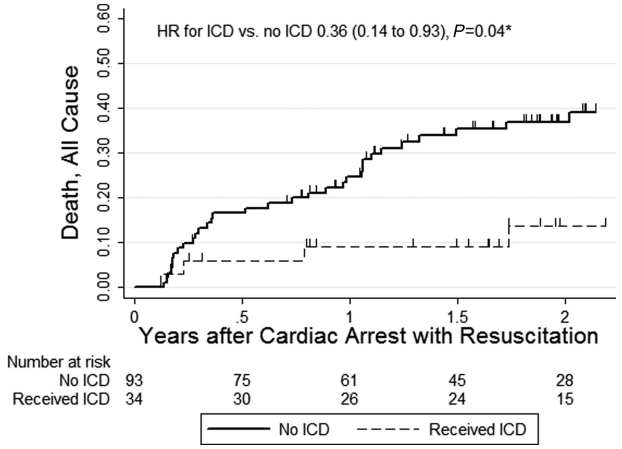

Figure. Kaplan–Meier survival curves for patients with and without an implantable cardioverter-defibrillator (ICD) implantation after cardiac arrest with resuscitation. *In the final step-wise Cox proportional hazards regression analysis, only age and ICD placement remained significant and were included in the model. HR indicates hazard ratio.

Our findings were generally consistent with those from HAT and other trials regarding the circumstances of out-of-hospital cardiac arrest. The proportion of sudden death events that occurred at home in VALIANT was similar to that reported in HAT, whereas the proportion of events that occurred in hospital was slightly higher, likely reflecting the increased burden of symptomatic heart failure in the VALIANT population.[7,10–13] Initial ECG rhythm was ventricular tachycardia or ventricular fibrillation for the majority of patients who had recorded rhythm in our study, which lies on the higher end of the range reported in patients with out-of-hospital cardiac arrest.[9,11,20] These differences are likely due to different prevalences of ischemic heart disease and heart failure in the populations studied, as well as the selection bias that stems from the difficulty of fully characterizing all arrest events when many of them are not witnessed. Regardless, our results reinforce the facts that a high proportion of sudden death events in patients with prior MI occur at home, and that a substantial proportion of those events are preceded by symptoms and manifest initially as ventricular tachycardia or ventricular fibrillation.

Despite a high proportion of shockable rhythms associated with sudden death events at home, the availability of home AED in HAT was not associated with any benefit in overall survival. Our observation that a large proportion of at-home

sudden death events occur during sleep, and are thus unwitnessed, may shed light on this negative result. In our analysis, only 19% of patients who were determined to be asleep had witnessed events, compared with 70% of those who were awake. We were able to determine sleep status for fewer than half of the patients who had an event at home. Because we used a strict criterion of classifying patients as being sleeping only if they were witnessed or if they were found recumbent in bed, the observed relationship between circadian activities and witness status is likely true and generalizable. Given the known association between whether an event is witnessed and the outcome of resuscitation, our findings are also consistent with other studies that showed decreased survival during nighttime for patients with out-of-hospital cardiac arrest, especially in residential settings.[21,22] It is thus not surprising that bystander-dependent and location-restricted strategies of sudden death prevention, such as home AED, turned out to be ineffective. Future efforts for the prevention of sudden death in patients with MI who are not eligible for ICD therapy will require better risk stratification, including an improved understanding of how risk factors evolve over time.[23] Proposed interventions will need to demonstrate that their application can be consistent during high-risk time periods such as sleep, as has been suggested in the most recent registry of wearable cardioverter defibrillators.[24] For the subset of high-risk patients with reduced ejection fraction immediately after MI who are not eligible for ICD implantation, preventive strategies will also have to take into account the high proportion of early events that occur in hospital and are thus not amenable for home interventions, such as AED or a wearable cardioverter defibrillator.

Our analysis also showed significantly improved survival for patients who received an ICD after cardiac arrest with resuscitation, although the decision to implant an ICD was clinically based and subject to several important biases, the most significant being geographic location. A substantially higher proportion of patients who received an ICD were randomized in the United States, and differences in healthcare settings and processes of care may remain potential confounders despite statistical adjustment. In addition, given that this was a retrospective analysis based on a small, nonrandomized cohort, the decision to offer ICD therapy may be considerably influenced by other risk features that we failed to capture, and we may not be able to completely eliminate the potential survivor bias in the decision for ICD implantation despite statistical adjustment. Despite these limitations, taken together, our findings are consistent with previous trials that established the use of ICDs for secondary prevention of sudden death and can be considered illustrative of the efficacy for the use of this strategy in a real-world setting.[25–28]

As with all post hoc analyses, our findings were necessarily hypothesis generating. Despite the availability of source documentation for nearly all sudden death events, the level of detail regarding the circumstances of the events varied greatly by center and by geographic region, and individual data elements such as preceding activity and initial ECG rhythm were missing for a substantial number of patients, introducing potentially significant bias. In addition, although we used a standardized abstraction instrument, the primary descriptions of the data elements of interest did not follow any standardized criteria such as those commonly used to categorize out-of-hospital cardiac arrests.[29] Finally, despite adjudication performed by a blinded, central committee, misclassification of other causes of death (eg, reinfarction, myocardial rupture, or noncardiac) as sudden death is likely unavoidable, as has been suggested by recent reviews of autopsy series, including those from the VALIANT cohort.[30,31] Because the adjudication criteria excluded patients with immediate antecedent MI or heart failure as having sudden death, we may also have missed the many deaths from arrhythmia that occur in those settings.

Conclusions

Our data show that most sudden death events in patients with high-risk MI occurred at home, were often preceded by symptoms, and had ventricular tachycardia or ventricular fibrillation as the initial ECG rhythm. Location of event and sleep were shown to be strongly associated with whether an arrest was witnessed. The risk of death for patients who did not receive ICD therapy after cardiac arrest with resuscitation remained dramatically elevated. These findings have implication for future strategies to prevent sudden death in patients with MI who are otherwise not candidates for ICD.

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Disclosures

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CLINICAL PERSPECTIVE

Sudden unexpected death is a frequent catastrophic complication in patients after myocardial infarction. For patients such as those with reduced ejection fraction immediately after myocardial infarction who are not eligible for implantable cardioverter-defibrillator therapy, strategies for prevention have remained elusive. In this study, we explored the circumstances of sudden death events in patients with high-risk myocardial infarction. We showed that only half of sudden death events occurring at home were witnessed, in part because of a high proportion (≈50%) of events occurring during sleep. We also demonstrated that early after myocardial infarction there was an increased likelihood of sudden death events occurring in hospital (44% within the first 40 days versus 21% for the entire follow-up period). Taken together, these findings help to explain the lack of efficacy of home automatic external defibrillators and suggest that strategies for prevention in this patient population should take into account the circumstances of sudden death events. Finally, we assessed the outcomes of patients who were successfully resuscitated after cardiac arrest, illustrating the benefit of secondary prevention implantable cardioverter-defibrillator therapy (hazard ratio for death 0.36; $P=0.04$).