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Wearable Cardioverter–Defibrillator after Myocardial Infarction

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ABSTRACT

BACKGROUND

Despite the high rate of sudden death after myocardial infarction among patients with a low ejection fraction, implantable cardioverter–defibrillators are contraindicated until 40 to 90 days after myocardial infarction. Whether a wearable cardioverter–defibrillator would reduce the incidence of sudden death during this high-risk period is unclear.

METHODS

We randomly assigned (in a 2:1 ratio) patients with acute myocardial infarction and an ejection fraction of 35% or less to receive a wearable cardioverter–defibrillator plus guideline-directed therapy (the device group) or to receive only guideline-directed therapy (the control group). The primary outcome was the composite of sudden death or death from ventricular tachyarrhythmia at 90 days (arrhythmic death). Secondary outcomes included death from any cause and nonarrhythmic death.

RESULTS

Of 2302 participants, 1524 were randomly assigned to the device group and 778 to the control group. Participants in the device group wore the device for a median of 18.0 hours per day (interquartile range, 3.8 to 22.7). Arrhythmic death occurred in 1.6% of the participants in the device group and in 2.4% of those in the control group (relative risk, 0.67; 95% confidence interval [CI], 0.37 to 1.21; $P=0.18$). Death from any cause occurred in 3.1% of the participants in the device group and in 4.9% of those in the control group (relative risk, 0.64; 95% CI, 0.43 to 0.98; uncorrected $P=0.04$), and nonarrhythmic death in 1.4% and 2.2%, respectively (relative risk, 0.63; 95% CI, 0.33 to 1.19; uncorrected $P=0.15$). Of the 48 participants in the device group who died, 12 were wearing the device at the time of death. A total of 20 participants in the device group (1.3%) received an appropriate shock, and 9 (0.6%) received an inappropriate shock.

CONCLUSIONS

Among patients with a recent myocardial infarction and an ejection fraction of 35% or less, the wearable cardioverter–defibrillator did not lead to a significantly lower rate of the primary outcome of arrhythmic death than control. (Funded by the National Institutes of Health and Zoll Medical; VEST ClinicalTrials.gov number, NCT01446965.)

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THE INCIDENCE OF SUDDEN CARDIAC death is high during the early months after a myocardial infarction,^{1,3} particularly among patients with a low left ventricular ejection fraction.^{2,7} Implantable cardioverter-defibrillators (ICDs) reduce mortality among patients with a reduced ejection fraction when the devices are implanted months to years after myocardial infarction.⁸⁻¹⁰ However, two randomized trials did not show a long-term mortality benefit from ICDs that had been implanted immediately after myocardial infarction.^{11,12}

The wearable cardioverter-defibrillator may protect against sudden death during the immediate period after myocardial infarction, before ICD implantation is indicated under current guidelines (beginning 40 days after myocardial infarction or 90 days if the patient has undergone revascularization).^{13,14} Registries and case series involving high-risk patients have shown that wearable cardioverter-defibrillators are effective in terminating ventricular tachyarrhythmias.¹⁵⁻¹⁹ We conducted the Vest Prevention of Early Sudden Death Trial (VEST) — a multicenter, randomized, controlled trial — to determine the efficacy of a wearable cardioverter-defibrillator during the period before ICDs are indicated in patients who have had a myocardial infarction and have a reduced ejection fraction.

METHODS

TRIAL DESIGN AND OVERSIGHT

The trial protocol (available with the full text of this article at NEJM.org) was designed by the investigators and originally included two components: the VEST randomized trial and the observational Prediction of ICD Treatment Study (PREDICTS)²⁰; only the results of VEST are reported in this article. The protocol was approved by the institutional review boards of the University of California, San Francisco, and the other trial sites. Details of the history of the trial, the role of the sponsors, and the trial oversight are provided in Figure S1 and Tables S1, S2, and S3 in the Supplementary Appendix (available at NEJM.org).

The trial was initially funded by the National Institutes of Health, which appointed the members of the independent data and safety monitoring board, with additional support from Zoll Medical. After 2011, funding was provided exclu-

sively by Zoll Medical. Zoll Medical had no role in the trial design, the selection or supervision of trial centers, the analysis or interpretation of the data, the preparation of the manuscript, or the decision to submit the manuscript for publication. Zoll Medical did participate in site monitoring. The authors vouch for the completeness and accuracy of the data and for the fidelity of the trial to the protocol.

PARTICIPANTS

Patients who had been hospitalized with an acute myocardial infarction²¹ and who had an ejection fraction of 35% or less (assessed ≥ 8 hours after myocardial infarction) were enrolled within 7 days after hospital discharge. For patients who had undergone revascularization, the ejection fraction was assessed 8 or more hours after percutaneous coronary intervention (PCI) or 48 or more hours after coronary-artery bypass grafting. Patients were excluded if they had an ICD or unipolar pacemaker, had clinically significant valve disease, were undergoing long-term hemodialysis, or had a chest circumference that was too small or too large to accommodate the wearable cardioverter-defibrillator. Patients were also excluded if they were pregnant or had been discharged to a nursing facility with an anticipated stay of more than 7 days. The inclusion and exclusion criteria are provided in Table S4 in the Supplementary Appendix. All the participants provided written informed consent.

TRIAL PROCEDURES

Eligible participants were randomly assigned in a 2:1 ratio to receive a wearable cardioverter-defibrillator plus guideline-directed medical therapy (the device group)²²⁻²⁷ or to receive guideline-directed medical therapy alone (the control group) at hospital discharge. The Zoll LifeVest wearable cardioverter-defibrillator^{16-18,28,29} that was used in this trial was commercially available in the United States and Germany (Fig. S2 in the Supplementary Appendix). Participants in the device group were fitted with the device, trained in its use, and instructed to wear the device continuously for 3 months (except while bathing). Sites were alerted if a participant wore the device for less than 15 hours in a 24-hour period (monitored through the device itself). Arrhythmias that were detected by the device were not reported to treating physicians or the trial sites unless a shock

was delivered or cardiac arrest occurred. Per protocol, crossovers from the control group to the wearable cardioverter-defibrillator were not allowed, and early ICD implantation (<3 months) was allowed only for guideline-based secondary prevention of sudden death.^{14,30,31}

FOLLOW-UP AND OUTCOMES

Participants were followed at 1 month with a telephone call and at 3 months with an in-person visit. At the conclusion of the trial, the National Death Index was searched for U.S. participants for whom vital status was unknown.

Initially, the primary outcome of the trial was death from any cause at 60 days; however, slower-than-expected recruitment made the originally planned sample of 4506 patients infeasible. On January 29, 2010, after the first 244 participants had been enrolled, the data and safety monitoring board, the steering committee, and the institutional review boards approved a change in the primary outcome to the combined 90-day incidence of sudden death and nonsudden death due to ventricular tachyarrhythmia; we refer to this outcome as arrhythmic death. The cause of death was adjudicated by an independent panel of experts who were unaware of the group assignments (and therefore did not have any data from the wearable cardioverter-defibrillator). With the revised primary outcome, the sample-size target was changed to 1890 (see the Supplementary Appendix). In October 2015, on the basis of lower-than-expected device wear time and without the inspection of outcome differences according to trial group^{32,33} (as prespecified in the protocol), the data and safety monitoring board recommended increasing the sample to 2300 patients.

Secondary outcomes were death from any cause; nonarrhythmic death; hospitalization for myocardial infarction, atrial fibrillation, congestive heart failure, stroke, or sustained ventricular tachyarrhythmia; wearable cardioverter-defibrillator wear time (as monitored by the device); and adverse events (Table S5 in the Supplementary Appendix). Definitions for the adjudicated outcomes are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

The primary analysis was performed according to the intention-to-treat principle. In the primary

analysis, participants who had an indeterminate cause of death were assumed not to have had arrhythmic death but were counted in the outcome of death from any cause, and all the participants with missing vital status were assumed to be alive. The primary outcome as well as death from any cause, nonarrhythmic death, and rehospitalization were compared with the use of unadjusted log-binomial models (with relative risks reported), with P values assessed by Pearson chi-square tests. Time-to-event analyses were conducted with the use of Cox models and are reported as Kaplan-Meier plots with hazard ratios. Rare events (indeterminate cause of death and other clinically significant arrhythmias — nonatrial fibrillation and nonventricular tachyarrhythmias) were analyzed with the use of exact logistic regression. The risk of having an alarm indicating arrhythmia was estimated with the use of random-effects logistic models to account for within-person clustering. P values are reported without correction for multiple comparisons, except where noted. Additional analyses, including sensitivity analyses to account for missing data, survival analyses (performed with the Kaplan-Meier method), P value corrections for multiple comparisons, and as-treated analyses are described in the Supplementary Appendix.

RESULTS

CHARACTERISTICS OF THE PARTICIPANTS

From July 2008 through April 2017, we enrolled 2348 participants at 76 sites in the United States, at 24 in Poland, at 6 in Germany, and at 2 in Hungary (Table S6 in the Supplementary Appendix). One U.S. site was dismissed on June 24, 2014, and the 46 participants at that site were excluded from the analyses, owing to irregularities found by the institutional review board at that site.

Therefore, a total of 2302 participants were included in the analyses (1524 participants in the device group and 778 in the control group) (Fig. S3 in the Supplementary Appendix). The two groups were balanced with regard to the participants' demographic characteristics, medical history, and characteristics of the index hospitalization for myocardial infarction (Table 1). The mean ejection fraction was 28%, and 83.6% of the participants underwent PCI during the index hospitalization. Table S7 in the Supplementary

Table 1. Characteristics of the Participants.*

Characteristic	Device Group (N=1524)	Control Group (N=778)
Age — yr	60.9±12.6	61.4±12.3
Male sex — no./total no. (%)	1108/1521 (72.8)	577/772 (74.7)
Body-mass index†	28.4±5.5	28.4±5.5
Race or ethnic group — no./total no. (%)‡		
White	1279/1491 (85.8)	636/751 (84.7)
Black	143/1491 (9.6)	75/751 (10.0)
Asian	23/1491 (1.5)	14/751 (1.9)
Native American or Alaskan	25/1491 (1.7)	12/751 (1.6)
Pacific Islander or Hawaiian	1/1491 (0.1)	0/751
Multiple	20/1491 (1.3)	14/751 (1.9)
Hispanic	85/1521 (5.6)	34/772 (4.4)
Baseline condition before index hospitalization — no./total no. (%)		
Current smoking	561/1520 (36.9)	273/770 (35.5)
Diabetes mellitus	497/1521 (32.7)	246/776 (31.7)
Hypertension	994/1521 (65.4)	501/776 (64.6)
Previous myocardial infarction	380/1518 (25.0)	193/775 (24.9)
Previous CABG	133/1521 (8.7)	70/776 (9.0)
Previous PCI	374/1520 (24.6)	202/776 (26.0)
Previous congestive heart failure	247/1518 (16.3)	146/774 (18.9)
NYHA functional class		
I	691/1520 (45.5)	326/775 (42.1)
II	529/1520 (34.8)	286/775 (36.9)
III	211/1520 (13.9)	116/775 (15.0)
IV	46/1520 (3.0)	18/775 (2.3)
Index hospitalization for myocardial infarction		
Left ventricular ejection fraction§		
Mean	28.2±6.1	28.2±5.8
Distribution — no./total no. (%)		
<25%	301/1519 (19.8)	148/777 (19.0)
25 to 35%	1217/1519 (80.1)	627/777 (80.7)
>35%	1/1519 (0.1)	2/777 (0.3)
PCI during index hospitalization — no./total no. (%)	1275/1513 (84.3)	650/773 (84.1)
Thrombolytic agent during index hospitalization — no./total no. (%)	118/1513 (7.8)	71/773 (9.2)
CABG during index hospitalization — no. (%)	14 (0.9)	12 (1.5)
Cardiac arrest or ventricular fibrillation — no./total no. (%)	169/1513 (11.2)	70/773 (9.1)
Pulmonary edema leading to intubation — no./total no. (%)	162/1513 (10.7)	88/773 (11.4)
Intraaortic balloon pump — no./total no. (%)	173/1513 (11.4)	93/773 (12.0)
Cardiogenic shock — no./total no. (%)	136/1513 (9.0)	79/773 (10.2)
Atrial fibrillation during hospitalization — no./total no. (%)	156/1513 (10.3)	91/773 (11.8)
Median maximum creatinine level (IQR) — mg/dl¶	1.1 (0.9–1.3)	1.1 (0.9–1.4)
Median no. of days from admission to randomization (IQR)	5.0 (3.0–8.0)	5.0 (3.0–7.0)

* Plus–minus values are means ±SD. There were no significant differences ($P<0.05$) between the trial groups. Percentages may not total 100 because of rounding. CABG denotes coronary-artery bypass grafting, IQR interquartile range, NYHA New York Heart Association, and PCI percutaneous coronary intervention.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ Race and ethnic group were reported by the participant.

§ An ejection fraction of 35% or less was an inclusion criterion for the study. An ejection fraction of more than 35% represents a protocol violation.

¶ To convert values for creatinine to micromoles per liter, multiply by 88.4.

Appendix shows the baseline characteristics of the participants who were enrolled before versus after the protocol was amended to change the primary outcome.

INTERVENTION AND TREATMENT

The majority of the participants in each group received guideline-directed medical therapy for myocardial infarction and heart failure (Table 2). In the device group, 43 participants (2.8%) never wore the device after randomization; in the control group, 20 participants (2.6%) received the device outside the protocol. Including person-days in which the wearable cardioverter-defibrillator was not worn at all, participants in the device

group wore the device for a median of 18.0 hours per day (interquartile range, 3.8 to 22.7) and for a mean (\pm SD) of 14.0 ± 9.3 hours per day (Table 2), with decreasing use over time. Details are provided in Figures S3 and S4 in the Supplementary Appendix. There was no significant between-group difference in the rate of ICD implantation during the follow-up period, nor was there a significant between-group difference in the timing of or reason for implantation (Table 2, and Table S8 in the Supplementary Appendix).

FOLLOW-UP AND OUTCOMES

The mean follow-up was 84.3 ± 15.6 days. A total of 10 participants (0.7%) in the device group and

Table 2. Treatment Received during the Trial Period.*

Treatment	Device Group (N=1524)	Control Group (N=778)	P Value
Wearable cardioverter-defibrillator			
Patients with device — no. (%)†	1481 (97.2)	20 (2.6)	<0.001
Hours per day that device was worn during follow-up‡			
Median (IQR)	18.0 (3.8–22.7)	0.0 (0.0–0.0)	<0.001
Mean	14.0 \pm 9.3	0.4 \pm 2.7	<0.001
Implantable cardioverter-defibrillator			
Patients with device — no. (%)§	67 (4.4)	44 (5.7)	0.18
Median no. of days from randomization to implantation (IQR)	62 (24–81)	58 (25–77)	0.33
Medication use — no. (%)¶			
Aspirin	1329 (87.2)	678 (87.1)	0.97
Other antiplatelet agent	1379 (90.5)	680 (87.4)	0.02
Statin	1386 (90.9)	696 (89.5)	0.25
Beta-blocker, including carvedilol	1411 (92.6)	720 (92.5)	0.97
ACE inhibitor or ARB	1334 (87.5)	667 (85.7)	0.23
Eplerenone or spironolactone	662 (43.4)	343 (44.1)	0.77
Other diuretic agent	736 (48.3)	385 (49.5)	0.59
Amiodarone	106 (7.0)	55 (7.1)	0.92
Other antiarrhythmic agent of class IA, IC, or III	5 (0.3)	4 (0.5)	0.50
Digoxin	86 (5.6)	44 (5.7)	0.99

* P values were not corrected for multiple comparisons. ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.

† The use of any wearable cardioverter-defibrillator by participants in the control group was a protocol violation.

‡ The number of hours per day that the wearable cardioverter-defibrillator was worn included follow-up days after discharge from the hospital and before death or implantable cardioverter-defibrillator (ICD) implantation and also included participants who did not wear it at all (0 hours per day on those days) in the two groups in order to describe the difference in the device coverage according to group. A total of 11 participants (4 in the device group and 7 in the control group) who died before discharge from the hospital were excluded from this analysis.

§ The implantation of an ICD in a participant in either group before 90 days of follow-up, unless for acceptable clinical indications for secondary prevention (e.g., cardiac arrest or sustained ventricular tachycardia during follow-up), was a protocol violation (Table S6 in the Supplementary Appendix).

¶ Participants provided details regarding medication use at follow-up visits.

12 (1.5%) in the control group were lost to follow-up, and their vital status at 90 days was unknown. An additional 2 participants in each group had insufficient data to determine whether the cause of death was arrhythmic or nonarrhythmic; therefore, they were considered to have had an indeterminate cause of death.

There was no significant difference between the two groups in the primary outcome of ar-

rhythmic death (1.6% in the device group and 2.4% in the control group; relative risk, 0.67; 95% confidence interval [CI], 0.37 to 1.21; $P=0.18$) (Table 3 and Fig. 1). The total mortality was 3.1% in the device group, as compared with 4.9% in the control group (relative risk, 0.64; 95% CI, 0.43 to 0.98; uncorrected $P=0.04$). The rate of nonarrhythmic death was 1.4% in the device group and 2.2% in the control group

Table 3. Primary, Secondary, and Other Outcomes.*

Event	Device Group (N=1524)	Control Group (N=778)	Relative Risk (95% CI)	P Value
Arrhythmic death				
No. of patients (%)†	25 (1.6)	19 (2.4)	0.67 (0.37–1.21)	0.18
Device worn at time of death or event leading to death — no.	9	0	NA	
Nonarrhythmic death				
No. of patients (%)‡	21 (1.4)	17 (2.2)	0.63 (0.33–1.19)	0.15
Device worn at time of death or event leading to death — no.	2	0	NA	
Indeterminate death				
No. of patients (%)§	2 (0.1)	2 (0.3)	0.51 (0.04–7.05)	0.83
Device worn at time of death or event leading to death — no.	1	0	NA	
Death from any cause				
No. of patients (%)	48 (3.1)	38 (4.9)	0.64 (0.43–0.98)	0.04
Device worn at time of death or event leading to death — no.	12	0	NA	
Rehospitalization, by cause — no. (%)¶				
Any	475 (31.2)	253 (32.5)	0.96 (0.85–1.09)	0.51
Cardiovascular or trial-related cause	335 (22.0)	174 (22.4)	0.98 (0.84–1.16)	0.83
Recurrent myocardial infarction	53 (3.5)	32 (4.1)	0.85 (0.55–1.30)	0.44
Stroke	14 (0.9)	8 (1.0)	0.89 (0.38–2.12)	0.80
Congestive heart failure	87 (5.7)	52 (6.7)	0.85 (0.61–1.19)	0.35
Ventricular tachycardia or ventricular fibrillation	24 (1.6)	20 (2.6)	0.61 (0.34–1.10)	0.10
Atrial fibrillation	8 (0.5)	5 (0.6)	0.82 (0.27–2.49)	0.72
Other clinically significant arrhythmia	8 (0.5)	3 (0.4)	1.36 (0.33–8.00)	0.92

* For common outcomes (including for the primary outcome of arrhythmic death and for other outcomes with at least five events in each group), a simple Pearson chi-square test was used to obtain P values, and log-binomial regression was used to estimate a relative risk with confidence intervals. For rare outcomes (<5 events in one or both groups), P values and relative risks were estimated with the use of exact logistic regression under the assumption that odds ratios produced by logistic regression are good estimates of relative risk when the outcome is rare. P values were not corrected for multiple comparisons. Details regarding the deaths or events leading to death that occurred while the participant was wearing the device are provided in Table S12 in the Supplementary Appendix. NA denotes not applicable.

† The primary outcome of arrhythmic death included sudden death and nonsudden death due to ventricular tachyarrhythmia.

‡ Nonarrhythmic death included all the deaths that did not meet the criteria for either arrhythmic death or indeterminate death (see below).

§ When documentation was inadequate for characterization of deaths as arrhythmic or nonarrhythmic, they were categorized as being indeterminate. Details are provided in the Supplementary Appendix.

¶ Site investigators were instructed to report all the hospitalization events occurring during follow-up if they were for conditions related to the heart or major arteries or to a trial procedure. These events were adjudicated for the presence of myocardial infarction, stroke, congestive heart failure, ventricular tachycardia or ventricular fibrillation, and other clinically significant arrhythmia with the use of standard criteria (see the Supplementary Appendix). Investigators were also asked to report the number of hospitalization events for any cause; these events were not adjudicated.

(relative risk, 0.63; 95% CI, 0.33 to 1.19; uncorrected $P=0.15$). With most approaches to correction for multiple testing, the P value for the analysis of total mortality was not significant (Table S9 in the Supplementary Appendix).

Results from the prespecified weighted sensitivity analyses to account for participants with unknown vital status or an indeterminate cause of death were similar to those of the primary analyses (Table S10 in the Supplementary Appendix). Analyses that were adjusted for the differences in length of follow-up owing to protocol changes were also similar to the main outcome analyses (Table S11 in the Supplementary Appendix). We found no significant between-group differences in the rates of other secondary events (Table 3).

Among the 48 participants in the device group who died, 12 were wearing the device at the time of death, including 9 of the 25 participants who had arrhythmic death (Table S12 in the Supplementary Appendix). Of these 9 participants, 4 had had a ventricular tachyarrhythmia detected and had received appropriate shocks with conversion to sinus rhythm but with subsequent recurrent ventricular tachyarrhythmias or agonal rhythms. In the remaining participants, no tachyarrhythmias were recorded. One other participant received an appropriate shock and underwent ICD implantation but died 2 weeks later with ventricular tachyarrhythmia storm. A total of 6 participants who died while wearing the device had asystole events (>3-second pause) during death (in 2 participants, these were preceded by multiple ventricular tachyarrhythmia episodes and shocks), which may represent terminal rhythms.

An as-treated analysis showed a rate of arrhythmic death of 0.37 per 100 person-months of wearing the device, as compared with a rate of 0.86 per 100 person-months of not wearing

Figure 1. Time-to-Event Curves for the Primary Outcome and Two Secondary Outcomes.

The primary outcome was a composite of sudden death or death due to ventricular tachyarrhythmia (Panel A). Secondary outcomes included nonarrhythmic death (Panel B) and death from any cause (Panel C). P values were not corrected for multiple comparisons. Insets show the same data on an enlarged y axis.

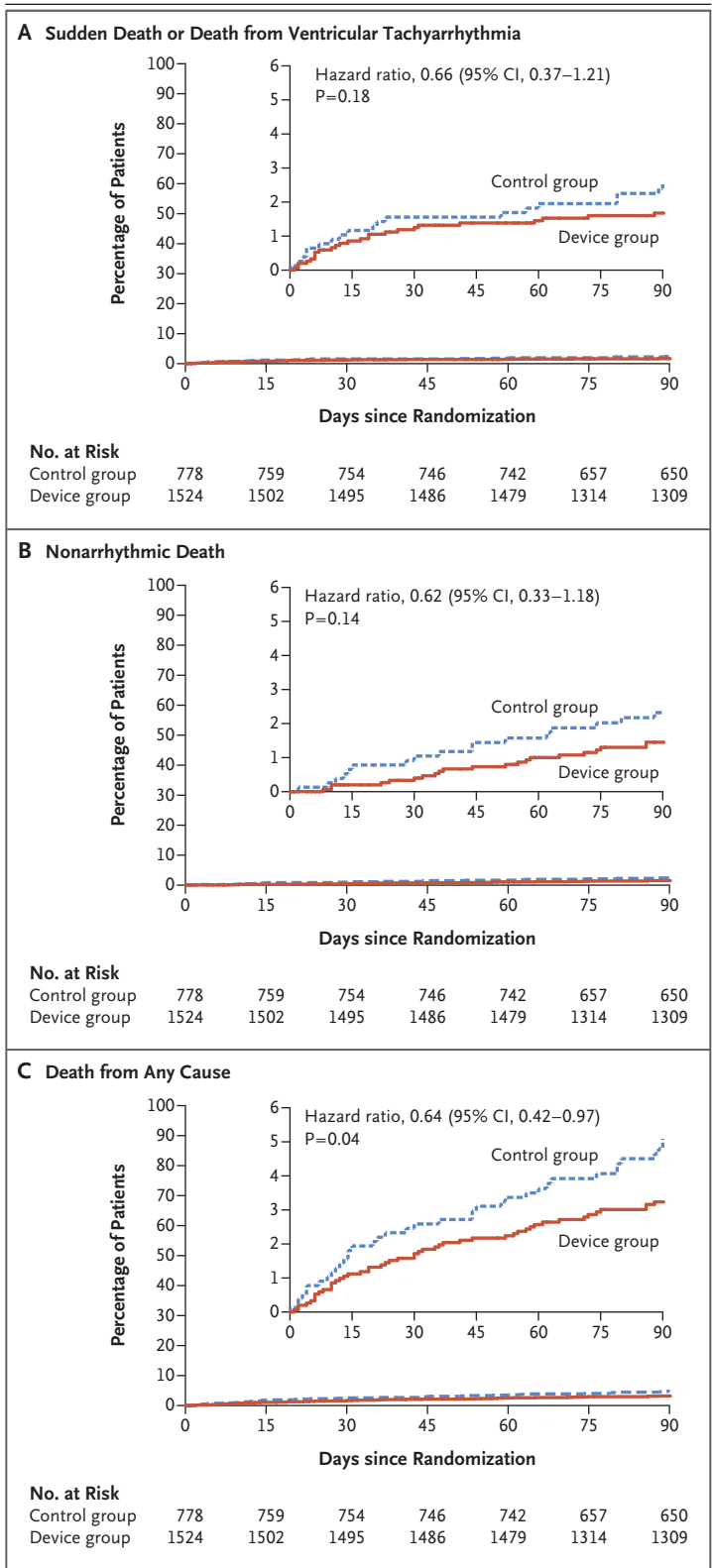


Table 4. Wearable Cardioverter–Defibrillator Therapies and Alarms.*

Variable	Device Group (N=1524) <i>no. of participants with event (%)</i>	Control Group (N=778)	P Value
No. of total shocks			<0.001
0	1495 (98.1)	777 (99.9)	
1	20 (1.3)	0	
≥2	9 (0.6)	1 (0.1)	
No. of appropriate shocks			0.008
0	1504 (98.7)	777 (99.9)	
1	13 (0.9)	0	
≥2	7 (0.5)	1 (0.1)	
No. of inappropriate shocks			0.12
0	1515 (99.4)	778 (100)	
1	7 (0.5)	0	
≥2	2 (0.1)	0	
No. of shocks aborted by pressing response button†			<0.001
0	1455 (95.5)	777 (99.9)	
1	43 (2.8)	1 (0.1)	
2–5	11 (0.7)	0	
>5	15 (1.0)	0	
No. of alarms indicating arrhythmia			<0.001
0	432 (28.3)	762 (97.9)	
1	115 (7.5)	1 (0.1)	
2–5	252 (16.5)	2 (0.3)	
6–100	579 (38.0)	12 (1.5)	
>100	146 (9.6)	1 (0.1)	
No. of alarms indicating asystole			<0.001
0	1483 (97.3)	777 (99.9)	
1	22 (1.4)‡	0	
≥2	19 (1.2)‡	1 (0.1)	

* Shown are the numbers of participants who had an event over the entire 90-day period. The wearable cardioverter–defibrillator was used by 20 participants in the control group, who received the device outside the protocol. Percentages may not total 100 because of rounding. P values were not corrected for multiple comparisons.

† This analysis included arrhythmia alarms lasting more than 30 seconds that were aborted when the participant pressed the shock-suppression button.

‡ Among 41 participants with an alarm indicating asystole, 6 events (all in the device group) were adjudicated as having had a true asystole event.

the device (rate ratio, 0.43; 95% CI, 0.21 to 0.91; uncorrected P=0.03) (see the Supplementary Appendix). An as-treated analysis of total mortality showed a rate of 0.50 per 100 person-months of wearing the device, as compared with a rate of 1.91 per 100 person-months of not wearing the device (rate ratio, 0.26; 95% CI, 0.14 to 0.48; Bonferroni corrected P<0.001). Adjustment for age, education, ejection fraction, and revascular-

ization had minimal effects. Potential biases in the as-treated analyses are discussed in the Supplementary Appendix.

SAFETY AND ADVERSE EVENTS

During a total of 1,765,772 hours of wearable cardioverter–defibrillator wear time, participants received 57,451 alarms for possible arrhythmias (as determined by the device algorithms); the

average rate (number of alarms ÷ total wear time in hours) was 0.033 alarms per hour. With adjustment for clustering of alarms according to day and within participant, the chance that a participant would have at least 1 arrhythmia alarm during 24 hours of wear time was 10.8% (95% CI, 9.8 to 11.9). Overall, accounting for crossovers and variable time worn, arrhythmia alarms (both false and true detections) occurred in 72% of the participants in the device group and in 2% of those in the control group, with 9.6% of participants in the device group being exposed to more than 100 alarms over the 90-day period (Table 4). The median duration of the arrhythmia alarm was 7 seconds (interquartile range, 3 to 12).

A total of 29 participants in the device group received at least one shock from the wearable cardioverter-defibrillator (Table 4); 20 participants (1.3%) received at least one appropriate shock, and 9 (0.6%) received at least one inappropriate shock. Of the 21 participants who received an appropriate shock (20 in the device group and 1 in the control group), 6 died (all in the device group). A total of 69 participants in the device group aborted shocks by pressing the patient-response buttons during an alarm; 3 of these participants subsequently received appropriate shocks within a few minutes but died, and 1 other participant died 12 hours later, after an appropriate shock (Table S12 in the Supplementary Appendix).

Four adverse events were potentially related to the wearable cardioverter-defibrillator (Table S13 in the Supplementary Appendix). Three were hospitalizations (two for aborted shocks and one for an inappropriate shock), and one was a death while the participant was wearing the device, which was deemed likely to not be an arrhythmic death (no tachyarrhythmia was recorded by the device and emergency medical technicians noted pulseless electrical activity on arrival).

A higher proportion of participants in the device group than in the control group reported itch and rash ($P < 0.001$). A lower proportion of participants in the device group than in the control group reported shortness of breath ($P = 0.004$). Details are provided in Table S14 in the Supplementary Appendix.

DISCUSSION

VEST compared the use of a wearable cardioverter-defibrillator plus guideline-directed medical therapy with guideline-directed medical ther-

apy alone in patients who presented with an acute myocardial infarction with an ejection fraction of 35% or less. During follow-up, we observed cardiac event rates that were similar to those in previous studies.^{3,4,6,11,12} The wearable cardioverter-defibrillator did not lead to a rate of arrhythmic death during the first 90 days — the primary outcome of the trial — that was significantly lower than the rate with guideline-directed medical therapy alone.

The trial may have been underpowered to detect a beneficial effect of the wearable cardioverter-defibrillator on the primary outcome. Our power calculation anticipated a 58% lower rate of arrhythmic death with the device than without it. The power was, in part, reduced because 5% of the deaths were adjudicated as being of indeterminate cause and were thus removed from the primary analysis. Misclassification of the adjudicated cause of death may have further reduced the power for the primary outcome. It is difficult to determine an arrhythmic cause of death accurately for unwitnessed deaths or deaths with limited documentation. In the Valsartan in Acute Myocardial Infarction (VALIANT) trial, only half the patients with sudden death who underwent autopsy were found to have died from arrhythmic death.³⁴ In a recent study that used a definition of sudden death that was similar to the definition in our trial but that also used autopsy as a standard for determining cause of death, only 56% of the presumed sudden cardiac deaths were found to be of arrhythmic origin.³⁵ In our trial, five of nine participants with adjudicated arrhythmic death who were wearing the device during the event had no ventricular tachyarrhythmias (adjudicators were unaware of the arrhythmia data from the device).

The original primary outcome of the trial was death from any cause; for this outcome, the uncorrected P value for comparison was 0.04 in favor of the wearable cardioverter-defibrillator. However, this result was not corrected for multiple testing, and given the use of most such corrections, the difference between the device and control groups would not be significant. Thus, the conservative interpretation is that this result was a chance finding. As with the primary outcome, the trial may have been underpowered to detect a beneficial effect of the device with regard to all-cause mortality. Although there is no clear mechanism to explain a benefit of the wearable cardioverter-defibrillator on non-

arrhythmic death, it is often difficult to determine an arrhythmic cause of death, as noted above.

As described previously,¹⁵⁻¹⁷ the wearable cardioverter–defibrillator was effective at converting ventricular tachyarrhythmias, with successful conversion in all 20 participants in the device group who received an appropriate shock, 14 of whom survived to 90 days (Table S12 in the Supplementary Appendix). Nonadherence to wearing the device may have reduced the power of the trial to show the effectiveness of this treatment strategy for the prevention of arrhythmic death. The power calculation assumed a device-adherence rate of 70%, a goal that was met or exceeded in the first 2 weeks after randomization but that waned over time (Fig. S4 in the Supplementary Appendix). It is also evident that some patients who are successfully treated with an appropriate shock subsequently die; not all successful defibrillations prolong survival. However, in an as-treated analysis, a significantly lower percentage of patients died when they were wearing the wearable cardioverter–defibrillator than when they were not, a finding that remained significant even after the most conservative correction for multiple comparisons. Although this result is subject to bias, it suggests a benefit to wearing the device (see the Supplementary Appendix) and implies that low adherence to wearing the device may be a limiting factor in the potential benefit of the wearable cardioverter–defibrillator.

Guidelines for primary prevention of sudden death with ICD implantation recommend waiting 40 days after an acute myocardial infarction

and 90 days after revascularization. Randomized trials have shown no benefit to ICD implantation early after an acute myocardial infarction.^{11,12} However, mortality was high during this vulnerable period, even with guideline-directed medical therapy and revascularization. We observed that mortality at 90 days was 4.9% in the control group, despite 84% of the participants having undergone PCI for acute myocardial infarction and more than 85% being treated with guideline-directed medical therapy. It remains unclear how to reduce the risk of arrhythmic death definitively, beyond what is possible with appropriate medical therapy, in the early period after myocardial infarction before ICDs are indicated.

In conclusion, in this trial, we compared the use of a wearable cardioverter–defibrillator plus guideline-directed medical therapy with guideline-directed medical therapy alone in patients who presented with an acute myocardial infarction with an ejection fraction of 35% or less. The wearable cardioverter–defibrillator did not result in a significantly lower rate of arrhythmic death than medical therapy during the first 90 days.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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