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Delayed Time to Defibrillation after In-Hospital Cardiac Arrest

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ABSTRACT

BACKGROUND

Expert guidelines advocate defibrillation within 2 minutes after an in-hospital cardiac arrest caused by ventricular arrhythmia. However, empirical data on the prevalence of delayed defibrillation in the United States and its effect on survival are limited.

METHODS

We identified 6789 patients who had cardiac arrest due to ventricular fibrillation or pulseless ventricular tachycardia at 369 hospitals participating in the National Registry of Cardiopulmonary Resuscitation. Using multivariable logistic regression, we identified characteristics associated with delayed defibrillation. We then examined the association between delayed defibrillation (more than 2 minutes) and survival to discharge after adjusting for differences in patient and hospital characteristics.

RESULTS

The overall median time to defibrillation was 1 minute (interquartile range, <1 to 3 minutes); delayed defibrillation occurred in 2045 patients (30.1%). Characteristics associated with delayed defibrillation included black race, noncardiac admitting diagnosis, and occurrence of cardiac arrest at a hospital with fewer than 250 beds, in an unmonitored hospital unit, and during after-hours periods (5 p.m. to 8 a.m. or weekends). Delayed defibrillation was associated with a significantly lower probability of surviving to hospital discharge (22.2%, vs. 39.3% when defibrillation was not delayed; adjusted odds ratio, 0.48; 95% confidence interval, 0.42 to 0.54; $P < 0.001$). In addition, a graded association was seen between increasing time to defibrillation and lower rates of survival to hospital discharge for each minute of delay (P for trend < 0.001).

CONCLUSIONS

Delayed defibrillation is common and is associated with lower rates of survival after in-hospital cardiac arrest.

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BETWEEN 370,000 AND 750,000 HOSPITALIZED patients have a cardiac arrest and undergo cardiopulmonary resuscitation each year in the United States, with less than 30% expected to survive to discharge.¹ Among the leading causes of cardiac arrest among adults during a hospitalization are ventricular fibrillation and pulseless ventricular tachycardia from primary electrical disturbances or cardiac ischemia.²⁻⁴ In contrast to cardiac arrests due to asystole or pulseless mechanical activity, survival from cardiac arrests due to ventricular fibrillation or pulseless ventricular tachycardia is improved if defibrillation therapy is administered rapidly.^{1,2,4}

Current recommendations are that hospitalized patients with ventricular fibrillation or pulseless ventricular tachycardia should receive defibrillation therapy within 2 minutes after recognition of cardiac arrest.^{5,6} Previous studies have suggested an association between time to defibrillation and survival, but the inclusion of cardiac arrests not amenable to defibrillation in most studies remains a potential confounder of this association.⁷⁻¹⁰ Moreover, the extent to which delayed defibrillation occurs in U.S. hospitals and its potential effect on survival are unclear.

Accordingly, we examined how often delayed defibrillation occurred during in-hospital cardiac arrests caused by ventricular arrhythmias and investigated the relationship between delayed defibrillation and survival, using data from the National Registry of Cardiopulmonary Resuscitation (NRCPR). The NRCPR is a large registry of U.S. hospitals that uses standardized Utstein definitions (a template of uniform reporting guidelines developed by international experts) to assess both processes of care and outcomes during in-hospital cardiac arrests.^{6,11-15} It provides a unique resource for exploring these questions as well as identifying key patient and hospital characteristics associated with delayed defibrillation.

METHODS

STUDY DESIGN

The study design of the NRCPR has been described in detail.⁴ Briefly, the NRCPR is a prospective, multicenter registry of in-hospital cardiac arrests that collects data according to standardized Utstein definitions.^{6,11-15} Cardiac arrest is defined as cessation of cardiac mechanical activity as determined by the absence of a palpable central pulse, apnea, and unresponsiveness. The NRCPR protocol spec-

ifies that all consecutive patients with cardiac arrests and without do-not-resuscitate orders be screened by dedicated staff at participating hospitals. Cases are identified by centralized collection of cardiac-arrest flow sheets, reviews of hospital paging-system logs, routine checks for use of code carts (carts stocked with emergency equipment), and screening for code-cart charges from hospital billing offices.

Accuracy of data in the NRCPR is ensured by certification of research staff, use of case-study methods for newly enrolled hospitals before submission of data, and a periodic reabstraction process, which has been demonstrated to have a mean error rate of 2.4% for all data.⁴ All patients are assigned a unique code during a single hospitalization, and data are transmitted to a central repository (Digital Innovation) without identification of the patient. Oversight of data collection and analysis, integrity of the data, and research is provided by the American Heart Association. The institutional review board of the University of Michigan Medical School approved this study and waived the requirement for written informed consent.

PATIENT POPULATION

Our analysis included 369 acute care hospitals that provided data for at least 6 months between January 1, 2000, and July 31, 2005. In patients 18 years of age or older, we identified 14,190 cases of in-hospital cardiac arrest in which the first identifiable rhythm was ventricular fibrillation or pulseless ventricular tachycardia (Fig. 1). If a patient had multiple cardiac arrests during the same hospitalization, we excluded data from subsequent episodes (involving 1587 recurrent arrests) to focus on the index event. We also limited our study population to patients whose cardiac arrests occurred while they were in intensive care units (ICUs) or inpatient beds. Because of the distinctive clinical circumstances associated with other hospital environments, we excluded a total of 3291 patients who were in emergency departments, operating rooms, procedure areas (cardiac catheterization, electrophysiology, and angiography suites), and postprocedural areas at the time of their cardiac arrest. Finally, we excluded patients with implantable cardioverter-defibrillators (170 patients), those who were receiving intravenous infusions of acute cardiac life support protocol medications for pulseless ventricular tachycardia or ventricular fibrillation (epinephrine, amiodarone, lidocaine, or

procainamide) at the time of cardiac arrest (1565 patients), and patients for whom data on the time of the cardiac arrest or defibrillation were missing (766 patients) or inconsistent (22 patients). The patients who were excluded because of missing or inconsistent time data had baseline characteristics that were similar to those of patients in the final study cohort, except that the excluded patients had lower rates of previous myocardial infarction (21.2% vs. 27.5%, $P < 0.001$) and higher rates of septicemia (13.6% vs. 11.2%, $P = 0.05$). The final study sample consisted of 6789 patients (Fig. 1).

TIME TO DEFIBRILLATION

The time to defibrillation was calculated as the interval from the reported time of initial recognition of the cardiac arrest to the reported time of the first attempted defibrillation. Both reported times were determined from cardiac-arrest documentation in the patient’s medical records and recorded in minutes. In our primary analysis, we used these data to determine the proportion of study subjects with delayed defibrillation, which was defined as a time to defibrillation greater than 2 minutes. In addition, we classified the study subjects according to whether their defibrillation time was 1 minute or less, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, or more than 6 minutes.

END POINTS

The primary outcome for our analysis was survival to hospital discharge. We also evaluated three secondary outcomes: return of spontaneous circulation for at least 20 minutes after onset of the cardiac arrest, survival at 24 hours after the cardiac arrest, and neurologic and functional status at discharge. Neurologic and functional status were assessed among survivors to discharge according to previously developed performance categories.¹⁶ For both neurologic and functional status, outcomes were categorized as no major disability, moderate disability, severe disability, or coma or vegetative state; data on these outcomes were available for 84% of survivors to hospital discharge. Patients whose data were missing did not differ significantly from those without missing data with regard to likelihood of delayed defibrillation (19.5% vs. 19.1%, $P = 0.85$).

STATISTICAL ANALYSIS

Unadjusted analyses evaluated baseline differences between patients with and without delayed defi-

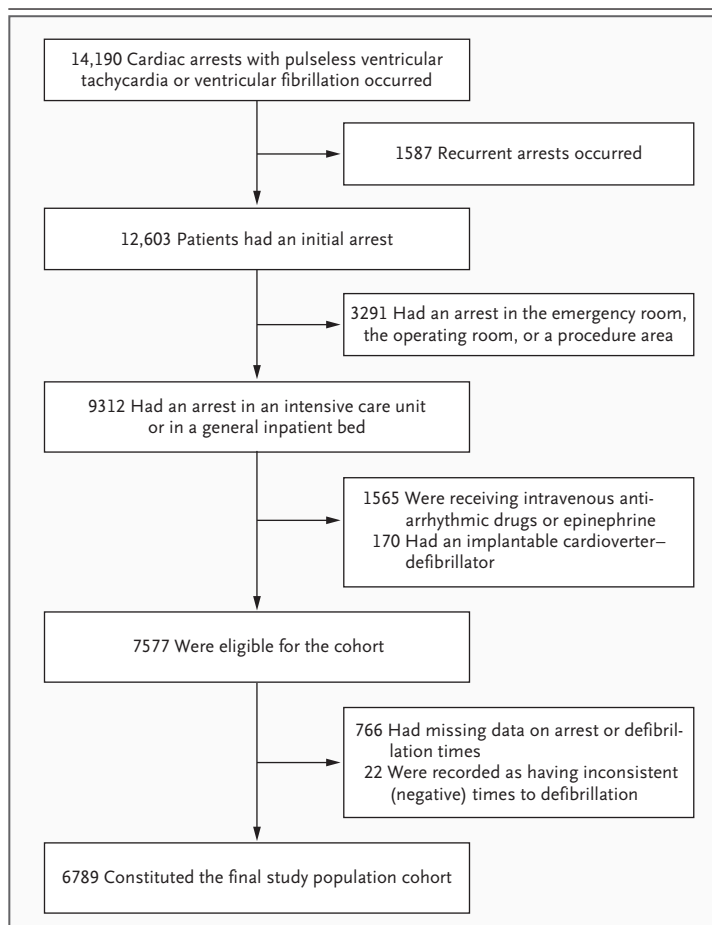


Figure 1. Study Cohort.

Of the initial 14,190 cases of in-hospital cardiac arrest due to pulseless ventricular tachycardia or ventricular fibrillation listed in the National Registry of Cardiopulmonary Resuscitation, 6789 eligible patients were included in the final study population.

brillation using Student’s t-test for continuous variables and the chi-square test for categorical variables. Multivariable logistic-regression models were used to examine the relationship between individual baseline characteristics and delayed defibrillation.

Multivariable models were then created to investigate the relationship between delayed defibrillation and outcomes. All models included age, sex, race (white, black, Hispanic, Asian or Pacific Islander, or Native American), and time to defibrillation (delayed or not delayed) as covariates. Additional candidate variables were selected from the following list after they had been determined to have a significant univariate association ($P < 0.05$) with survival: initial cardiac rhythm (ventricular fibrillation or pulseless ventricular tachycardia),

admitting diagnosis (medical, cardiac; medical, noncardiac; surgical, cardiac; or surgical, noncardiac), presence or absence of congestive heart failure or myocardial infarction at the time of admission, presence or absence of previous congestive heart failure or myocardial infarction, presence or absence of coexisting medical conditions at the time of cardiac arrest (respiratory, renal, or hepatic insufficiency; metabolic or electrolyte derangements; diabetes mellitus; baseline evidence of motor, cognitive, or functional deficits; acute stroke; acute nonstroke neurologic disorder; pneumonia; sepsis; major trauma; or cancer), the use or nonuse of therapeutic interventions at the time of cardiac arrest (intraaortic balloon pump, pul-

monary-artery catheter, or hemodialysis), time of cardiac arrest (during work hours or during after-hours periods [i.e., 5 p.m. to 8 a.m. or weekend]), the use or nonuse of a hospital-wide cardiopulmonary-arrest (code blue) alert, type of hospital bed where the cardiac arrest occurred (ICU, inpatient bed monitored by telemetry, or unmonitored inpatient bed), and hospital size (<250, 250 to 499, or ≥500 inpatient beds). We also performed analyses to explore the relationship between time to defibrillation and survival to hospital discharge across a range of times.

All models used generalized estimating equations with an unstructured correlation matrix to account for the potential effects of clustering of

Table 1. Baseline Characteristics According to Time to Defibrillation.*

Characteristic	≤2 Minutes to Defibrillation (N = 4744)	>2 Minutes to Defibrillation (N = 2045)	P Value
Age — yr	67.9±13.9	67.6±14.8	0.49
Male sex — no. (%)	2876 (60.6)	1207 (59.0)	0.15
White race — no. (%)†	3608 (76.1)	1457 (71.2)	<0.001
Ventricular fibrillation — no. (%)	3276 (69.1)	1454 (71.1)	0.08
Hospital-wide code blue — no. (%)	4141 (87.3)	1889 (92.4)	<0.001
Type of hospital bed — no. (%)			<0.001
Intensive care	2910 (61.3)	816 (39.9)	
Inpatient, monitored by telemetry	1368 (28.8)	816 (39.9)	
Inpatient, unmonitored	466 (9.8)	413 (20.2)	
Hospital size — no. (%)			<0.001
<250 beds	1124 (23.7)	576 (28.2)	
250–499 beds	2178 (45.9)	886 (43.3)	
≥500 beds	1387 (29.2)	565 (27.6)	
Unknown	55 (1.2)	18 (0.9)	
Geographic region — no. (%)			0.38
Northeast	502 (10.6)	233 (11.4)	
Midwest	1352 (28.5)	550 (26.9)	
South	2135 (45.0)	920 (45.0)	
West	755 (15.9)	342 (16.7)	
Admitting diagnosis — no. (%)			<0.001
Medical, cardiac	2377 (50.1)	799 (39.1)	
Medical, noncardiac	1427 (30.1)	861 (42.1)	
Surgical, cardiac	508 (10.7)	145 (7.1)	
Surgical, noncardiac	432 (9.1)	240 (11.7)	
Time of cardiac arrest — no. (%)			
After hours‡	2650 (55.9)	1209 (59.1)	0.01
Weekend	1252 (26.4)	576 (28.2)	0.14

Table 1. (Continued.)

Characteristic	≤2 Minutes to Defibrillation (N=4744)	>2 Minutes to Defibrillation (N=2045)	P Value
Cardiac diagnosis — no. (%)			
Congestive heart failure at admission	1295 (27.3)	470 (23.0)	<0.001
Previous congestive heart failure	1404 (29.6)	623 (30.5)	0.44
Myocardial infarction at admission	1418 (29.9)	442 (21.6)	<0.001
Previous myocardial infarction	1252 (26.4)	503 (24.6)	0.16
Coexisting medical conditions — no. (%)			
Respiratory insufficiency	1703 (35.9)	712 (34.8)	0.39
Renal insufficiency	1542 (32.5)	679 (33.2)	0.69
Hepatic insufficiency	285 (6.0)	143 (7.0)	0.15
Metabolic or electrolyte derangement	792 (16.7)	346 (16.9)	0.95
Diabetes mellitus	1542 (32.5)	695 (34.0)	0.25
Baseline central nervous system deficits§	526 (11.1)	237 (11.6)	0.55
Acute stroke	176 (3.7)	90 (4.4)	0.21
Acute nonstroke neurologic disorder	318 (6.7)	131 (6.4)	0.51
Pneumonia	569 (12.0)	270 (13.2)	0.21
Sepsis	512 (10.8)	258 (12.6)	0.08
Major trauma	38 (0.8)	23 (1.1)	0.16
Cancer	432 (9.1)	219 (10.7)	0.05
Therapeutic interventions — no. (%)			
Intraaortic balloon pump	90 (1.9)	12 (0.6)	<0.001
Pulmonary-artery catheter	247 (5.2)	66 (3.2)	<0.001
Hemodialysis	161 (3.4)	72 (3.5)	0.83

* Plus-minus values are means ±SD.

† Race was determined by the hospital investigators.

‡ After hours was defined as before 8 a.m., after 5 p.m., or on weekends.

§ Central nervous system deficits included motor, cognitive, and functional deficits.

patients within hospitals. For all analyses, the null hypothesis was evaluated at a two-sided significance level of 0.05, with calculation of 95% confidence intervals. All analyses were performed with SAS software, version 9.1.

RESULTS

We identified 6789 patients from 369 hospitals who had in-hospital cardiac arrests due to ventricular fibrillation (69.7%) or pulseless ventricular tachycardia (30.3%). Overall, the median time to defibrillation was 1 minute (interquartile range, <1 to 3 minutes), with 2045 patients (30.1%) noted as having had delayed defibrillation according to our definition (a time to defibrillation greater than 2 minutes). Table 1 displays baseline characteris-

tics of patients with and of those without delayed defibrillation.

Table 2 lists characteristics significantly associated with delayed defibrillation in multivariate analysis. Patient factors associated with delayed defibrillation included black race and a noncardiac admitting diagnosis. Significant hospital-related factors included small hospital size (<250 beds), occurrence of cardiac arrest in an unmonitored inpatient bed, and occurrence of cardiac arrest after hours.

Return of spontaneous circulation occurred in 4168 patients (61.4%), 3372 patients (49.7%) survived to 24 hours after their cardiac arrest, and 2318 (34.1%) survived to hospital discharge. The unadjusted survival outcomes were significantly lower for patients with delayed defibrillation

Table 2. Factors Associated with Delayed Time to Defibrillation in Multivariable Analysis.*

Variable	Adjusted Odds Ratio (95% CI)	P Value†
Race or ethnic group‡		
White	Reference	Reference
Black	1.23 (1.05–1.43)	0.009
Hispanic	1.09 (0.83–1.43)	0.56
Asian or Pacific Islander	0.99 (0.83–1.43)	0.98
Native American	1.25 (0.61–2.57)	0.54
Unknown	1.02 (0.78–1.34)	0.11
After-hours cardiac arrest§	1.18 (1.05–1.33)	0.005
Type of hospital bed		
Intensive care unit	0.39 (0.33–0.46)	<0.001
Inpatient, monitored by telemetry	0.47 (0.41–0.53)	<0.001
Inpatient, unmonitored	Reference	Reference
Hospital size		
<250 beds	1.27 (1.08–1.47)	0.001
250–499 beds	1.02 (0.90–1.17)	0.72
≥500 beds	Reference	Reference
Admitting diagnosis		
Medical, cardiac	0.67 (0.55–0.82)	<0.001
Surgical, cardiac	0.67 (0.51–0.86)	0.002
Noncardiac	Reference	Reference

* Patient- and hospital-level variables that independently predicted a time to defibrillation of more than 2 minutes are shown. CI denotes confidence interval.

† P<0.01 for inclusion in the model.

‡ Race and ethnic group were determined by the hospital investigators.

§ After hours was defined as before 8 a.m., after 5 p.m., or on weekends.

(49.0% vs. 66.7% for return of spontaneous circulation, 37.4% vs. 55.0% for survival to 24 hours, and 22.2% vs. 39.3% for survival to hospital discharge) (Table 3). A graded inverse association was found between time to defibrillation and unadjusted survival across a broad range of time thresholds (Fig. 2).

After adjustment for patient- and hospital-related characteristics, delayed defibrillation was found to be associated with a significantly lower likelihood of survival to hospital discharge (adjusted odds ratio, 0.48; 95% confidence interval [CI], 0.42 to 0.54; P<0.001) (Table 3). When time to defibrillation was evaluated in discrete intervals, a graded inverse association was found between longer delays and survival, with a significantly lower likelihood of survival to hospital discharge with increased time to defibrillation (Fig. 2).

Delayed defibrillation was also associated with a significantly lower likelihood of return of spontaneous circulation (adjusted odds ratio, 0.55; 95% CI, 0.49 to 0.62; P<0.001) and survival at 24 hours after the cardiac arrest (adjusted odds ratio, 0.52; 95% CI, 0.46 to 0.58; P<0.001) (Table 3). These results remained robust when examined separately according to type of hospital bed (ICU, monitored inpatient, or unmonitored inpatient) (see the Supplementary Appendix, available with the full text of this article at www.nejm.org). Finally, among those surviving to discharge, delayed defibrillation was associated with a significantly lower likelihood of having no major disabilities in neurologic status (adjusted odds ratio, 0.74; 95% CI, 0.57 to 0.95; P=0.02) or functional status (adjusted odds ratio, 0.74; 95% CI, 0.56 to 0.96; P=0.02) (Table 3).

DISCUSSION

We found that 30.1% of patients with cardiac arrests due to ventricular arrhythmia underwent defibrillation more than 2 minutes after initial recognition of their cardiac arrest, a delay that exceeds guidelines-based recommendations.^{5,6} Patients with delayed defibrillation were significantly less likely to survive to hospital discharge. Among survivors, patients with delayed defibrillation were less likely to have no major disabilities in neurologic or functional status. These findings support the conclusion that rapid defibrillation is associated with sizable survival gains in these high-risk patients. Furthermore, we found a graded association between poorer survival and longer times to defibrillation, even for times beyond 2 minutes. These observations reinforce the rationale for efforts to shorten the time to defibrillation as much as possible to maximize the effectiveness of resuscitation of patients with ventricular fibrillation or pulseless ventricular tachycardia.

Our work confirms and extends the findings of other investigations that have shown a relationship between defibrillation time and survival. Although earlier studies linked delayed defibrillation to poorer survival in hospitalized patients, most of these reports included heterogeneous study populations (i.e., both patients with “shockable” and those with “unshockable” rhythms, such as asystole, at the time of cardiac arrest).^{7,9,10} Moreover, these studies were generally small and involved a limited number of hospitals. In contrast, our analysis focused only on patients with cardiac

Table 3. Summary of Study End Points and Adjusted Survival Rates with Delayed Defibrillation.*

End Point	≤2 Minutes to Defibrillation (N=4744)	>2 Minutes to Defibrillation (N=2045)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)†	P Value
Survival outcomes — no./total no. (%)					
Return of spontaneous circulation	3165/4744 (66.7)	1003/2045 (49.0)	0.48 (0.43–0.53)	0.55 (0.49–0.62)	<0.001
Survival to 24 hr	2607/4744 (55.0)	765/2045 (37.4)	0.48 (0.43–0.54)	0.52 (0.46–0.58)	<0.001
Survival to discharge	1863/4744 (39.3)	455/2045 (22.2)	0.44 (0.39–0.50)	0.48 (0.42–0.54)	<0.001
Neurologic outcomes — no./total no. (%)‡					
No major disability	931/1549 (60.1)	197/381 (51.7)		0.71 (0.57–0.89)	0.02
Moderate disability	437/1549 (28.2)	134/381 (35.2)			
Severe disability	152/1549 (9.8)	36/381 (9.4)			
Coma or vegetative state	29/1549 (1.9)	14/381 (3.7)			
Functional outcomes — no./total no. (%)‡					
No major disability	533/1542 (34.6)	100/381 (26.2)	0.67 (0.52–0.87)	0.74 (0.56–0.96)	0.02
Moderate disability	638/1542 (41.4)	164/381 (43.0)			
Severe disability	342/1542 (22.2)	103/381 (27.0)			
Coma or vegetative state	29/1542 (1.9)	14/381 (3.7)			

* Patients for whom the time to defibrillation was more than 2 minutes had lower unadjusted and adjusted survival rates, as well as lower rates of survival to discharge with intact neurologic and functional status, than those for whom the time was 2 minutes or less. CI denotes confidence interval.
 † Odds ratios are adjusted for age, sex, race, initial cardiac rhythm, admitting diagnosis, presence or absence of congestive heart failure and myocardial infarction at admission, presence or absence of previous congestive heart failure and myocardial infarction, presence or absence of coexisting medical conditions at the time of cardiac arrest, use or nonuse of a hospital-wide code blue, use or nonuse of treatment interventions (intraaortic balloon pump, pulmonary-artery catheter, and hemodialysis), type of hospital bed, and hospital size.
 ‡ Neurologic and functional outcomes are given only for those who survived until hospital discharge. Model comparisons were made between survivors discharged with no major disability and those with a moderate degree of disability or worse.

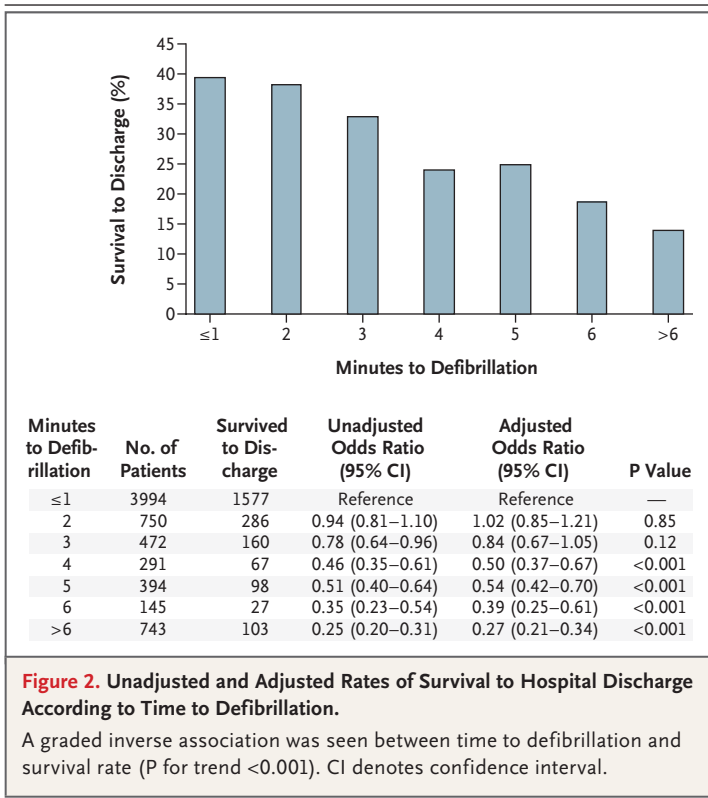
arrest due to ventricular fibrillation or pulseless ventricular tachycardia and excluded other potentially inappropriate patients, such as those receiving concomitant treatment with intravenous antiarrhythmic or vasoactive infusions or those with preexisting implantable cardioverter-defibrillators. The large size of the NRCPR and its use of standardized definitions were instrumental in this regard.

Several factors related to the hospital setting were associated with delayed defibrillation, including the occurrence of a cardiac arrest after hours or in an unmonitored inpatient bed. These findings imply that response times may be related, in part, to the emergent availability of trained medical personnel, access to defibrillation equipment, and delays in recognition of a ventricular arrhythmia.

In addition to hospital-related factors, certain patient characteristics were found to be associated with a greater likelihood of delayed defibrillation. The relationship between a cardiac admit-

ting diagnosis and shorter time to defibrillation is probably due to earlier recognition of the ventricular arrhythmia. However, the association of black race with delayed defibrillation is not intuitively obvious and raises potential issues of disparities in care. Further studies are warranted to determine whether such variations are due to geographic differences in access to hospitals with more resources (such as more monitored beds) or whether they reflect actual differences in practice patterns according to race.

Our study should be interpreted in the context of the following limitations. First, although data available in the NRCPR allowed us to adjust for key variables that have been linked to survival after cardiac arrest, our study used an observational design, and there are variables that we did not or could not capture (for example, a physician's a priori assessment of the likelihood of survival or good neurologic outcome in an arrest). These additional factors may influence time to defibrillation, leading to residual confounding.



Second, data on time to defibrillation relied on reported times of cardiac arrest and defibrillation from hospital records. The use of multiple clocks and the lack of synchronization between the timing of cardiac monitors and defibrillators within a hospital may lead to variability and discrepancies in calculating time to defibrillation.^{17,18} This variability in measurement would be expected to bias our findings toward the null hypothesis, suggesting that we may be underestimating the association between delayed defibrillation and sur-

vival. In addition, because time to defibrillation was recorded in minutes, our analysis primarily explored its association with survival at the skewed upper end of this variable's distribution. The effect of time to defibrillation within short intervals of less than a minute could not be assessed.

Third, the results related to neurologic and functional status should be interpreted with caution, since these data were missing for 16% of patients surviving to hospital discharge. Finally, although hospitals in the NRCPR represent nearly 15% of the large hospitals (>250 beds) in the United States, their participation is voluntary. Performance characteristics, quality of care, and survival outcomes may be different in nonparticipating hospitals.

In conclusion, we found that delays in the time to defibrillation are common in hospitalized patients with cardiac arrest due to a ventricular arrhythmia, and we identified several patient- and hospital-related factors associated with delayed time to defibrillation. In our analysis, such delays were associated with substantially worse clinical outcomes, with each additional minute of delay resulting in worse survival.

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APPENDIX

The American Heart Association National Registry of Cardiopulmonary Resuscitation investigators are as follows: G. Nichol, M. Mancini, R. Berg, M.A. Peberdy, E. Allen, S. Braithwaite, J. Gosbee, E. Hunt, G.L. Larkin, G. Mears, V. Nadkarni, T. Truitt, J. Potts, B. Abella, R. Geocadin, K. Kern, B. Eigel, and J. Ornato.

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