

A Program Encouraging Early Defibrillation Results in Improved In-Hospital Resuscitation Efficacy

A. Maziar Zafari, MD, PhD, FACC,*† Susan K. Zarter, RN,† Vicki Heggen, RN,†
Patricia Wilson, RN, MSN,† Regina A. Taylor, RN,† Kiran Reddy, BA,*† Andrea G. Backscheider, PhD,‡
Samuel C. Dudley, Jr, MD, PhD, FACC*†

Atlanta, Georgia

OBJECTIVES	The purpose of this study was to determine whether survival to discharge after in-hospital cardiopulmonary arrest could be improved by a program encouraging early defibrillation that included switching from monophasic to biphasic devices.
BACKGROUND	In-hospital resuscitation continues to have a low success rate. Biphasic waveform devices have demonstrated characteristics that might improve survival, and outside the hospital, automated external defibrillators (AEDs) have shown promise in improving survival of patients suffering cardiopulmonary arrest.
METHODS	A program including education and replacement of all manual monophasic defibrillators with a combination of manual biphasic defibrillators used in AED mode and AEDs in all outpatient clinics and chronic care units was implemented.
RESULTS	With program implementation, the percentage survival of all patients with resuscitation events improved 2.6-fold, from 4.9% to 12.8%. Factors independently predicting survival included event location outside an intensive care unit, younger age, an initial rhythm of pulseless ventricular tachycardia (VT) or ventricular fibrillation (VF), pre-arrest beta-blocker, and program initiation. The outcome was independent of gender, race, work shift, number of previous resuscitation attempts, body mass index, comorbidity index, presence of diabetes, presence of hypertension, or use of angiotensin-converting enzyme inhibitors. The improvement in mortality was attributable solely to an effect on patients presenting with VT/VF. Patients with these initial rhythms were 14-fold (odds ratio = 0.07 of death, confidence interval = 0.02 to 0.3) more likely to survive to discharge after program initiation. Automated external defibrillators performed similarly to biphasic manual defibrillators in AED mode.
CONCLUSIONS	A program including education and use of biphasic manual defibrillators in AED mode and selective use of AEDs improved survival to discharge in hospitalized patients suffering from cardiopulmonary arrest. (J Am Coll Cardiol 2004;44:846–52) © 2004 by the American College of Cardiology Foundation

Cardiopulmonary resuscitation (CPR) has been practiced for more than 40 years (1). Although it has become standard in hospital settings and is performed on a large number of patients, there is a wide variation in the reported survival to

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discharge, ranging from 0% to 28.9%, with an average survival rate in hospital-wide populations around 10% (2–8). There was no temporal trend observed in reported in-hospital CPR survival between January 1972 through November 1994 (4). Previous studies have shown that

survival is correlated with the speed with which definitive therapies such as CPR and defibrillation are begun after cardiac arrest (9). Bedell et al. (10) reported in 1983 a 27% discharge rate (26 patients) of 97 patients resuscitated with ventricular tachycardia (VT)/ventricular fibrillation (VF) in a university teaching hospital. Nevertheless, the likelihood of survival after cardiac arrest is heavily dependent on the severity of each patient's illness. Studies in geriatric populations or in cancer patients had fewer survivors than those conducted in hospital-wide populations. Likewise, survival rates from in-hospital resuscitation are considerably lower in Veterans Affairs hospitals, which generally admit older patients or patients with more severe and complex medical problems than patients from a community hospital (7). Few procedural changes in CPR responses have been studied or have shown efficacy in improving survival (11). Factors known to influence survival in out-of-hospital arrests are early defibrillation and bystander CPR (12–15). Newer biphasic waveform devices have shown characteristics that suggest they might improve survival, but data to support this conclusion have been lacking (16–19). The role of automated external defibrillators (AED) in this setting is still

From *Emory University School of Medicine, Department of Medicine, Division of Cardiology, Atlanta, Georgia; †Atlanta Veterans Administration Medical Center, Division of Cardiology, Atlanta, Georgia; ‡Atlanta Veterans Administration Medical Center, Health Services Research and Development, Atlanta, Georgia. Funded, in part, by Philips Medical Systems, N.A., who also provided the initial automated external defibrillators, and by the Atlanta Veterans Affairs Medical Center, Health Services Research and Development Program. Dr. Dudley was supported by a National Institutes of Health (NIH) grant, a VA MERIT grant, and a Scientist Development Award from the American Heart Association. Dr. Zafari was supported by a grant from the Southeast Affiliate American Heart Association.

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Abbreviations and Acronyms

ACE	=	angiotensin-converting enzyme
AED	=	automated external defibrillator
BMI	=	body mass index
CPR	=	cardiopulmonary resuscitation
DNR	=	Do Not Resuscitate
ICU	=	intensive care unit
VAMC	=	Veterans Administration Medical Center
VF	=	ventricular fibrillation
VT	=	ventricular tachycardia

controversial but promising, and there are no published manuscripts comparing their use to other devices.

We undertook a study to see if survival to discharge could be influenced by a program including replacement of conventional monophasic defibrillators with a combination of biphasic waveform manual defibrillators in AED mode and use of AEDs in all outpatient clinics and chronic care units. Our hypothesis was that this program involving use of biphasic waveform devices and AEDs in the hospital setting would be more effective in improving survival in patients with CPR events than the previous standard practice.

METHODS

Early defibrillation program. The program to enhance early defibrillation was instituted at the 291 bed Atlanta Veterans Administration Medical Center (VAMC) under a protocol approved by the Emory University Institutional Review Board under a multiproject agreement with the Atlanta VAMC. The program consisted of education of all nursing and medical staff and, starting on January 1, 2001, replacement of all 68 manual monophasic defibrillators by a combination of 34 Philips Medical Systems (Andover, Massachusetts) manual biphasic defibrillators used in AED mode and placed in high-use areas such as the intensive care units (ICUs) and 27 Philips AEDs in lower-use locations including all outpatient clinics and chronic care units. Automated external defibrillator output was fixed at 150 J. Both units had the same biphasic waveform with chest wall impedance compensation. Education consisted of repetitive education started in fall 2000 and included 70 workshops and hands-on training sessions for all nursing and medical staff designated to locations where AEDs were to be used. Additionally, 12 monthly lectures were given to the Emory University medical housestaff regarding role of early defibrillation in CPR. These lectures included hands-on training with AEDs. Finally, AED training was incorporated into the annual nursing skills assessments.

Study population. The study sample consisted of 569 consecutive patients who had an in-hospital cardiopulmonary arrest with resuscitation attempted between January 1, 1995, and June 30, 2002. Cardiopulmonary arrests that occurred in the emergency department were included only if the patient arrived at the center in a pre-arrest state. The medical records of all patients receiving CPR were exten-

sively reviewed to determine the presence of the following demographic data and clinical characteristics including age, race, body mass index (BMI), comorbid conditions, the presence of diabetes, the presence of hypertension, and the prescription of angiotensin-converting enzyme (ACE) inhibitors or beta-blockers at any time before arrest. Each record was assessed to determine whether the patient survived to discharge, the initial cardiac rhythm, the use of a defibrillator, the number of previous resuscitation attempts, the arrest location, the work shift when arrest occurred, and the neurological outcome for survivors as defined by the Glasgow-Pittsburgh Cerebral Performance Categories (20). The comorbidity index was calculated as the unweighted sum of the number of comorbidities as defined by the National Registry of Cardiopulmonary Resuscitation modified to include the diagnosis of preexisting hypertension. To enhance reporting uniformity, a single team member conducted all chart reviews, with 10% of the charts being randomly reviewed again. A detailed substudy of 60 randomly selected charts from arrest survivors was undertaken to determine measures of the intensity of a resuscitation effort as a function of year. Blinded analysis included the frequency of intubation, epinephrine use, and the duration of resuscitation efforts. All results after January 1, 2001, were reported to the National Registry for Cardiopulmonary Resuscitation.

Data analysis. The predefined primary outcome was survival to discharge. Demographic and clinical categorical and continuous variables were compared before and after the initiation of the early defibrillation program using chi-square tests and two-sample *t* tests, respectively. After combining data on all patients, a multiple logistic regression model was used to identify independent predictors of death by considering all the available variables: gender, race, age, BMI, comorbidity score, the presence of hypertension, the presence of diabetes, arrest date in relation to early defibrillation program initiation, initial rhythm, number of previous CPR events, work shift when CPR event occurred, location of arrest, and the prescription of ACE inhibitors before arrest, and the prescription of beta-blockers before the arrest. A forward stepwise selection procedure was used with a *p* value of at least 0.05 for entry and 0.10 for removal. All pairwise interactions between the early defibrillation program initiation and the other variables in the final stepwise model were tested. A Hosmer-Lemeshow test was used to test goodness of fit (test statistic = 6.36 on 8 degrees of freedom, *p* = 0.61). Odds ratios are presented with 95% confidence intervals. Means are presented \pm 1 SD. Statistical analyses were performed using SPSS version 11.5 (SPSS Inc., Chicago, Illinois).

RESULTS

There were a total of 569 in-hospital CPR events for the 90-month period between January 1, 1995, and June 30, 2002. Of these, 141 events occurred after program initia-

Table 1. Demographic and Clinical Characteristics of Study Subjects

	Time Period		p Value
	1995-2000	2001-June 2002	
Number of subjects*	428	141	
Age (yrs)	66.5 ± 12.2	65.4 ± 12.5	0.33
BMI	24.1 ± 6.2	25.5 ± 6.5	0.03
Comorbidity score	2.9 ± 1.5	3.0 ± 1.7	0.56
ACE inhibitors			0.003
Yes	170 (39.7%)	79 (56.0%)	
No	235 (54.9%)	61 (43.3%)	
Missing†	23 (5.4%)	1 (0.7%)	
Beta-blockers			0.001
Yes	101 (23.6%)	55 (39.0%)	
No	304 (71.0%)	85 (60.3%)	
Missing†	23 (5.4%)	1 (0.7%)	
Presence of diabetes			0.06
Yes	108 (25.2%)	50 (35.5%)	
No	286 (66.8%)	90 (63.8%)	
Missing†	34 (7.9%)	1 (0.7%)	
Presence of hypertension			0.37
Yes	205 (47.9%)	79 (56.0%)	
No	189 (44.2%)	61 (43.3%)	
Missing†	34 (7.9%)	1 (0.7%)	
Gender			0.004
Male	426 (99.5%)	136 (96.5%)	
Female	2 (0.5%)	5 (3.5%)	
Race			0.21
White	233 (54.4%)	91 (64.5%)	
Black	165 (38.6%)	50 (35.5%)	
Other/unknown‡	30 (7.0%)	0 (0.0%)	
Initial rhythm			0.57
VT/VF‡	73 (19.2%)	24 (17.0%)	
Other	307 (80.8%)	117 (83.0%)	
Defibrillated during CPR event			0.70
Yes	176 (47.3%)	64 (45.4%)	
No	196 (52.7%)	77 (54.6%)	
Shift when arrest occurred			0.23
Night	163 (40.0%)	59 (43.4%)	
Day	140 (34.4%)	52 (38.2%)	
Evening	104 (25.6%)	25 (18.4%)	
Location of arrest			0.09
Intensive care units	162 (37.9%)	47 (35.3%)	
General ward	204 (47.6%)	71 (53.4%)	
Other	45 (10.5%)	6 (4.5%)	
Emergency department	17 (4.0%)	9 (6.8%)	
Age (yrs)			0.09
≤65	177 (41.4%)	70 (49.6%)	
>65	251 (58.6%)	71 (50.4%)	

*Missing data for some variables precludes the total number of subjects from summing to the total reported; †chi-square test excluded these groups; ‡VT/VF indicates pulseless VT or VF.

ACE = angiotensin-converting enzyme; BMI = body mass index; CPR = cardiopulmonary resuscitation; VF = ventricular fibrillation; VT = ventricular tachycardia.

tion. Table 1 shows that no statistically significant differences in demographic and clinical characteristics existed between patient groups before or after program initiation except that patients after implementation were more likely to be female, have a higher BMI, and be prescribed ACE inhibitors and beta-blockers. In addition, there was a

Table 2. Outcomes Before and After Program Initiation

Outcome	Time Period		p Value
	1995-2000	2001-June 2002	
Alive at discharge	21 (4.9%)	18 (12.8%)	0.001
Died in hospital	407 (95.1%)	123 (87.2%)	
Neurological outcome*	1.72 ± 0.46	2.00 ± 0.43	0.36

*The Glasgow-Pittsburgh Cerebral Performance Categories: 1) good cerebral performance; 2) moderate cerebral disability; 3) severe cerebral disability; 4) coma, vegetative state; 5) death. The score was determined for survivors only.

marginally significant trend toward increased prevalence of diabetes in this group. The increase in females probably reflects general demographic trends within the Veterans Administration health system over this time period. The increase in BMI is also consistent with general demographic trends (21).

The program resulted in a substantial improvement in the primary outcome, survival to discharge (Table 2, Fig. 1). Our 18-month results show a 2.6-fold improvement in survival to discharge after program implementation (p = 0.001). The rate of survival to discharge after arrest before the implementation of the program was 4.9% for all patients with resuscitation attempts during a five-year period, which is comparable to a previously reported survival rate of 5.5% in another Veterans Administration hospital at a similar time period (7). With program implementation, our survival rate improved sharply to 12.8%. Among survivors, there was no difference in neurological status as measured by the Glasgow-Pittsburgh Cerebral Performance scores in which both groups averaged moderate cerebral impairment (i.e., a score of ~2; p = 0.36)

Logistical regression analysis revealed that age, location of CPR event, initial rhythm, prescription of beta-blockers before arrest, and AED program initiation were predictors of survival. Therefore, outcome was independent of gender, race, work-shift of occurrence, number of previous CPR attempts, BMI, comorbidity index, the presence of diabetes,

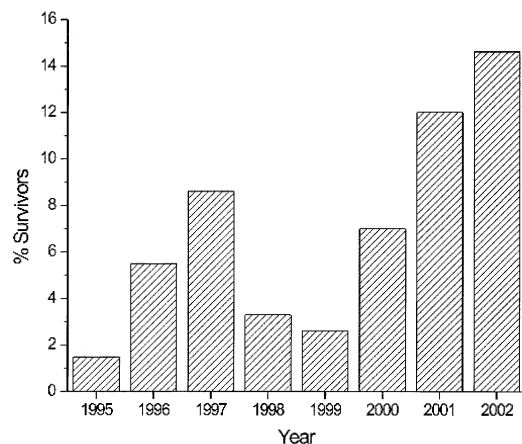


Figure 1. The percentage of arrest victims alive at discharge as a function of year. The percentage of patients surviving to discharge was greater after a program encouraging early defibrillation was instituted in 2001.

Table 3. Multiple Logistic Model for Variables Associated With Failure to Survive to Discharge

	Odds Ratio of Death	95% Confidence Interval	Wald p Value
Beta-blockers			
Not prescribed vs. prescribed	4.1	(1.7, 9.7)	0.001
Location of CPR event			
Intensive care units vs. general ward	2.4	(0.8, 7.2)	0.11
Intensive care units vs. emergency department	10.5	(2.5, 44.6)	0.001
Intensive care units vs. other	5.0	(1.2, 21.6)	0.03
Age			
Every 10-yr increase	1.6	(1.1, 2.2)	0.01
Initial rhythm			
VT/VF*			
Before vs. after program initiation	17.0	(2.9, 98.7)	0.002
Other			
Before vs. after program initiation	0.9	(0.3, 2.7)	0.85
Program initiation			
Before program initiation			
VT/VF vs. other	1.4	(0.3, 6.5)	0.70
After program initiation			
VT/VF vs. other	0.07	(0.02, 0.3)	<0.0003

*VT/VF indicates pulseless VT or VF.

CPR = cardiopulmonary resuscitation; VF = ventricular fibrillation; VT = ventricular tachycardia.

the presence of hypertension, and the use of ACE inhibitors. The final model is summarized in Table 3. Patients were 2.4- to 10.5-fold more likely to die in the hospital if they arrested in the ICUs than in any other location. For each decade of life, the odds ratio of death after an event increased by 1.6-fold (95% confidence interval, 1.1 to 2.2). The effect of age is similar to previous reports (7,22). Patients who were not being prescribed beta-blockers were 4.1-fold more likely to die (95% confidence interval, 1.7 to 9.7).

Consistent with an improvement in the efficacy of defibrillation, patients with the presenting rhythms of VF or pulseless VT were 17.0-fold (95% confidence interval, 2.9 to 98.7) more likely to die before program initiation. In contrast, patients with other presenting rhythms were equally likely to die before or after the start of the program (odds ratio = 0.9; 95% confidence interval, 0.3 to 2.7). Consistent with this observation, there was little difference in the odds ratio for death in patients with VT/VF before the program (odds ratio = 1.4; 95% confidence interval, 0.3 to 6.5), but VT/VF patients were 16.9-fold less likely to die (odds ratio = 0.07 for death; 95% confidence interval, 0.02 to 0.34) after program initiation. Figure 2 demonstrates that the percentage of arrest victims presenting with VT/VF alive at discharge was higher after program initiation in 2001. Notably, cardiac arrest victims with VT/VF had a 37.5% survival rate after program implementation.

Although the rates of defibrillation use during an arrest were similar, 47.3% versus 45.4% of cases before and after program implementation, biphasic defibrillation improved survival to discharge in defibrillated patients by more than sevenfold. There were a total of 64 patients who received defibrillation during CPR after program commencement, compared with 176 patients receiving defibrillation between 1995 and 2000. Among the 64 patients treated during the

program, 10 patients (15.6%) survived to discharge, compared with four survivors (2.2%) of 176 patients receiving defibrillation between 1995 and 2000. Of the 64 defibrillations after program initiation, 27 (42.2%) were performed by an AED and 37 (57.8%) by a manual biphasic defibrillator in AED mode. Survival to discharge was comparable for the AED group (14.8%, n = 4) and for the manual, biphasic defibrillator group (16.2%, n = 6) (Fig. 3).

DISCUSSION

This study provides evidence that, in the hospital setting, a program designed to enhance resuscitation survival and including biphasic waveform devices used in AED mode is safe and increases survival to discharge by 2.6-fold in patients with cardiopulmonary arrest. The improvement in

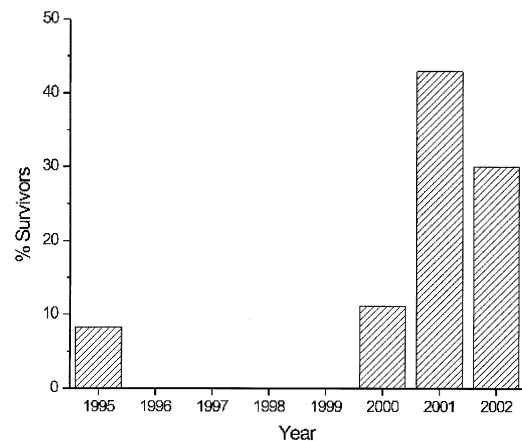


Figure 2. The percentage of the arrest victims presenting with pulseless ventricular tachycardia or ventricular fibrillation alive at discharge as a function of year. The percentage of patients presenting with life-threatening rhythms surviving to discharge was greater after a program encouraging early defibrillation was instituted in 2001.

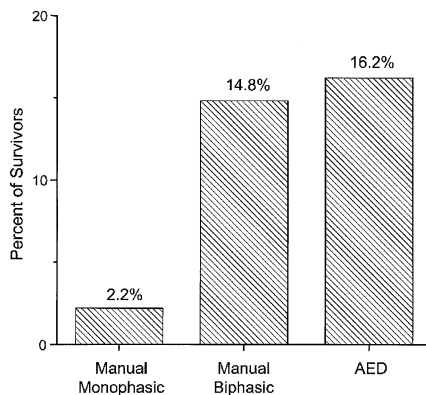


Figure 3. The percentage of survivors among patients receiving defibrillation with various types of devices. In the hospital setting, automated external defibrillators (AED) appeared equally effective to manual biphasic defibrillators but superior to manual monophasic defibrillators.

survival seemed to be mediated by an improvement in outcome of those patients presenting with VT/VF. While there was no statistical difference in the incidence of this presentation before or after program initiation, before program initiation patients with VT/VF were equally likely to die during CPR (odds ratio = 1.4; 95% confidence interval, 0.3 to 6.5). After program initiation, the odds ratio of death was reduced 14-fold (odds ratio = 0.07; 95% confidence interval, 0.02 to 0.3) for the VT/VF group when compared with all other patients. Neurological outcomes were comparable between groups. The better survival in patients presenting in VT/VF has been reported for in-hospital arrests by a number of other investigators (23–29).

In addition to program initiation and the presence of VT/VF, 3 of 15 other factors independently influenced survival to discharge. The odds ratio of death was increased in the ICUs versus other hospital areas. In our study, as in others (27,30), there was a higher odds ratio of death after arrest in the ICU, but our data showed no interaction between ICU location of arrest and the two cohorts, suggesting that the program was not differentially effective by hospital location. The increased likelihood of death in the ICU seems most likely attributable to factors other than the program, but it cannot be ruled out that ICU results could be improved with AEDs rather than manual defibrillators. The influence of beta-blockers may be similar to its effect on prevention of sudden death seen in other studies and is consistent with a recent animal study of resuscitation outcomes (31). Finally, similar to others (25–27,32–34), age was important also in determining survival to discharge in our population. The outcome was independent of gender, race, work-shift, number of previous resuscitation attempts, BMI, comorbidity index, presence of diabetes, or presence of hypertension. Although previously it has been reported that survival rates after out-of-hospital cardiac arrests are lower in blacks (0.8%) as compared with 2.6% in whites, our analysis shows no racial differences in utilization of early defibrillation between whites and blacks, as well as no

differences in survival to discharge after CPR in the hospital setting (35).

The validity of our results is enhanced because no patients were excluded from analysis, the primary outcome was available for all patients, the primary outcome was not subject to observer interpretation, and the results were both clinically and statistically significant. Given the relatively sick, aged population, community hospitals might expect an even better result with similar programs (5,36).

A limitation of this study is that the control group is historical rather than concurrent. This choice of control group was dictated largely by the difficulty of introducing multiple devices with differing energy settings during resuscitation in a hospital simultaneously. Nevertheless, we undertook several types of analysis to show that the groups were comparable and that other changes over time were unlikely to be responsible for the outcome improvement seen. There were some differences in the demographics of the two cohorts, but these are unlikely to explain the observed effect. Women have had either equivalent or improved outcomes during resuscitation in previous studies (37–45), and, while there is a paucity of data about obesity and CPR, obesity in general is associated with worse cardiovascular outcomes, a trend opposite to that seen in this study (46). The regression analysis supported the concept that these differences and that of ACE inhibitor use could not explain the change in outcome after program initiation. Moreover, there was no change in the use of Do Not Resuscitate (DNR) orders between the groups. Among all deaths in our hospital, the average percentage of patients that were DNR was 47% versus 42% before and after program initiation, respectively ($p = 0.88$).

It is possible that changes in the conduct of CPR over the course of this study confounded the results. To investigate this possibility, we undertook a detailed substudy of 60 randomly selected charts from arrest survivors. Blinded analysis did not reveal any substantial differences in the conduct of resuscitations as measured by the frequency of intubation, epinephrine use, and the duration of resuscitation efforts. This substudy did reveal differences in the pattern of use of defibrillators, however. The pre-implementation patients tended to receive a greater number of shocks (3.49 ± 2.8 vs. 2.06 ± 1.4) and more total energy ($1,064.1 \pm 1,014.9$ vs. 473.3 ± 437.3) than the post-implementation sample. When we examined the number of shocks and total energy used for the surviving and the deceased patients separately, the only significant difference was that the deceased patients in the pre-implementation group tended to have received more energy than the deceased patients in the post-implementation group (Mann-Whitney $U = 125.0$; $p = 0.023$).

Changes in amiodarone use before and after program initiation were analyzed and found to be insufficient to explain the observed improvement in survival. Amiodarone has been shown to improve survival to hospital admission in out-of-hospital arrests (47), but an increase in its use over

the course of this study is unlikely to explain fully the substantial improvement in mortality seen in our hospital-wide population. Amiodarone was not made available for use during CPR until October of 2001, but survival improvement correlated with program implementation. Of the 141 arrests during the program period, 27 patients were treated with amiodarone, and 5 survived to discharge (18.5%). In the patients resuscitated without use of amiodarone, 11.4% survived to discharge, a trend consistent with the previous out-of-hospital result, but both of these groups showed improvement in the primary outcome when compared with historical controls, in which amiodarone use would have been negligible.

Based on our study design, it is not possible to separate the roles of biphasic waveform technology, use of AEDs, and enhanced education on improvement in outcome, and further analysis in this regard will be necessary. It is possible that the improvement in survival was the result of a Hawthorne effect where increased education and awareness rather than the actual experimental conditions were responsible for the outcome. We cannot exclude that such is the case in our study, especially because significant education was part of the program. Nevertheless, it would be difficult to design a study that introduced new technology without education or that randomized people to AED versus manual defibrillator use within a single hospital. Our results should represent a realistic, obtainable program ready for implementation in the hospital setting. The fact that the benefits were ward-dependent argues that the effect is unlikely to be explained fully by education, which was equivalent throughout the hospital.

One possible reason for improved survival could be an improved time to defibrillation, and AEDs have improved the time to defibrillation in other settings (13,14). Obtaining accurate data on the interval from arrest onset to defibrillation is methodologically difficult. For this reason it is rarely reported in these types of trials and was not available in our study. Regardless, AED use in the hospital setting was safe and yielded results similar to manual biphasic defibrillators. Our findings are consistent with other literature suggesting that AEDs show substantial rates of survival after arrest in non-medical settings (12,14,48–50), but the equivalent performance of AEDs to manual biphasic defibrillators used in AED mode could be explained by the introduction of biphasic waveform devices. This could be tested in the future if true biphasic waveform AEDs improved survival in the ICU. Given increasing difficulties with staffing, the differences in level of expertise needed to operate the devices, and the cost differential, AEDs may be an attractive option for hospitals.

In summary, a hospital-based program to improve resuscitation efficacy that included the use of a combination of biphasic manual defibrillators operated in AED mode and selective placement of AEDs was safe and improved outcomes in patients with cardiopulmonary arrest compared with patients treated with monophasic manual defibrillators.

An initial rhythm of VT/VF, younger age, and the prescription of beta-blockers before arrest were independent predictors of likelihood of survival to discharge. Arrest in the ICU was associated with a higher odds ratio of death. Because of the study design using historical controls, the cause of improved resuscitation efficacy cannot be determined unambiguously. Future trials with concurrent controls will be necessary to define further the degree of resuscitation improvement that can be ascribed to the newer devices used in our trial.

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Reprint requests and correspondence: Dr. Samuel C. Dudley, Jr., Division of Cardiology, Emory University/VAMC, 1670 Clairmont Road (111B), Decatur, Georgia. E-mail: sdudley@emory.edu.

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