

Influence of Cardiopulmonary Resuscitation Prior to Defibrillation in Patients With Out-of-Hospital Ventricular Fibrillation

Leonard A. Cobb, MD

Carol E. Fahrenbruch, MSPH

Lt Thomas R. Walsh, NREMT-P

Michael K. Copass, MD

Michele Olsufka, RN

Maryann Breskin, MS

Alfred P. Hallstrom, PhD

THERE IS LITTLE DOUBT THAT SPEED in providing care represents the major determinant of survival for patients with out-of-hospital ventricular fibrillation (VF). That relationship has been documented for initiation of cardiopulmonary resuscitation (CPR)^{1,2} as well as for the arrival of personnel and devices necessary for defibrillation.^{3,4} Since 1970, the pattern for delivering out-of-hospital emergency care in Seattle, Wash, has incorporated rapidly responding first units staffed by emergency medical technicians (EMTs), followed as soon as possible by a later-arriving paramedic unit.⁵ In 1980, we initiated the use of early defibrillation by EMTs in 4 first-responding units.⁶ Later, automated external defibrillators (AEDs) were extensively used. Whereas the survival experience of subsets of VF patients in Seattle seemed to be improved with AEDs,⁷ the overall survival rate remained virtually unchanged (FIGURE 1) despite an approximately 3- to 4-

See also pp 1175 and 1220 and Patient Page.

Context Use of automated external defibrillators (AEDs) by first arriving emergency medical technicians (EMTs) is advocated to improve the outcome for out-of-hospital ventricular fibrillation (VF). However, adding AEDs to the emergency medical system in Seattle, Wash, did not improve survival. Studies in animals have shown improved outcomes when cardiopulmonary resuscitation (CPR) was administered prior to an initial shock for VF of several minutes' duration.

Objective To evaluate the effects of providing 90 seconds of CPR to persons with out-of-hospital VF prior to delivery of a shock by first-arriving EMTs.

Design Observational, prospectively defined, population-based study with 42 months of preintervention analysis (July 1, 1990-December 31, 1993) and 36 months of post-intervention analysis (January 1, 1994-December 31, 1996).

Setting Seattle fire department-based, 2-tiered emergency medical system.

Participants A total of 639 patients treated for out-of-hospital VF before the intervention and 478 after the intervention.

Intervention Modification of the protocol for use of AEDs, emphasizing approximately 90 seconds of CPR prior to delivery of a shock.

Main Outcome Measures Survival and neurologic status at hospital discharge determined by retrospective chart review as a function of early (<4 minutes) and later (≥ 4 minutes) response intervals.

Results Survival improved from 24% (155/639) to 30% (142/478) ($P = .04$). That benefit was predominantly in patients for whom the initial response interval was 4 minutes or longer (survival, 17% [56/321] before vs 27% [60/220] after; $P = .01$). In a multivariate logistic model, adjusting for differences in patient and resuscitation factors between the periods, the protocol intervention was estimated to improve survival significantly (odds ratio, 1.42; 95% confidence interval, 1.07-1.90; $P = .02$). Overall, the proportion of victims who survived with favorable neurologic recovery increased from 17% (106/634) to 23% (109/474) ($P = .01$). Among survivors, the proportion having favorable neurologic function at hospital discharge increased from 71% (106/150) to 79% (109/138) ($P < .11$).

Conclusion The routine provision of approximately 90 seconds of CPR prior to use of AED was associated with increased survival when response intervals were 4 minutes or longer.

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minute shortened time to defibrillatory shock in most cases. Such a time saving had been predicted to increase survival by several percentage points.³ Prompted by the lack of overall improvement in

Author Affiliations: Departments of Medicine (Drs Cobb, Fahrenbruch, Copass and Mss Olsufka Breskin) and Biostatistics (Dr Hallstrom), University of Washington, Harborview Medical Center, and the Seattle Fire Department (Lt Walsh), Seattle, Wash.

Corresponding Author and Reprints: Leonard A. Cobb, MD, Box 359748, Harborview Medical Center, Seattle, WA 98104 (e-mail: lcobb@u.washington.edu).

survival and by the experimental work of Niemann et al⁸ in which resuscitation rates improved when animals were pretreated with CPR and epinephrine, we modified the protocol for first-responding Seattle Fire Department EMTs. The revised protocol directed the provision of approximately 90 seconds of CPR before automated analysis of cardiac rhythm for patients found in cardiac arrest.

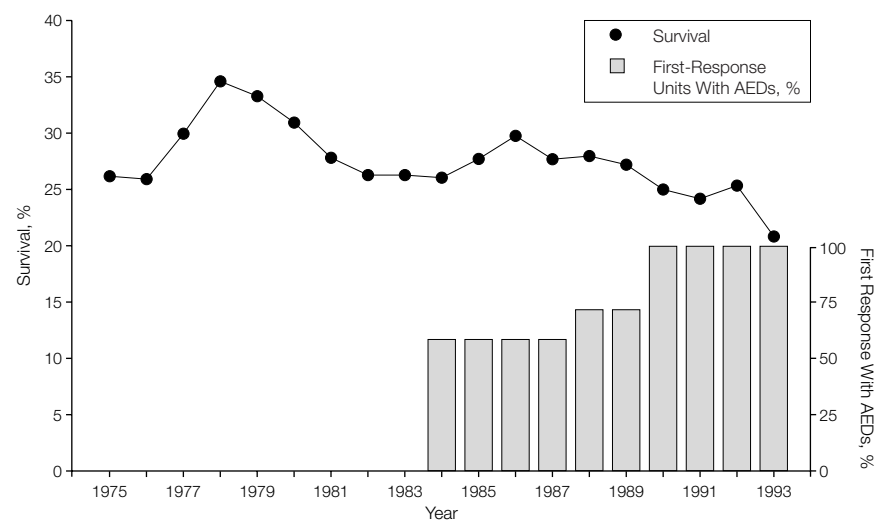
In this report, we compare outcomes during 2 contiguous periods of patients whose initial rhythm was VF. In the earlier period, emphasis had been directed to immediate defibrillation after minimal, if any, CPR by first-arriving EMTs. During the later period, initial CPR prior to defibrillation was emphasized.

METHODS

Since 1970, the outcomes of all patients treated for cardiac arrest in Seattle have been monitored.^{5,9} Beginning in 1984, most first-responding EMT units were equipped with AEDs (Physio-Control [Redmond, Wash] Lifepak 200 was used through September 1994; Lifepak 300 thereafter) and staffed by personnel trained to use those devices.^{7,10} Until early in 1994, immediate defibrillation was emphasized to the first arriving firefighters, although CPR was recommended if it could be carried out by available personnel while the AED was made ready. The 1984 standing orders stated, "Application of the automatic external defibrillator is to have the highest priority. . . ."

In February 1994, standing orders for first-arriving EMTs were modified to assign primary importance to the provision of basic life support prior to application of an AED. These orders stated, ". . . the designated CPR person will begin chest compressions immediately at a rate of 80 to 100 compressions per minute . . . to accomplish 150 compressions in 90 seconds." Virtually all patients received bag-mask ventilation—either from a third (ventilation-designated) person, if in attendance, or from the designated AED person after readying the device. The above

Figure 1. Annual (January 1-December 31) Survival Rates for Out-of-Hospital Ventricular Fibrillation in Seattle



A total of 4611 patients were treated from 1975 through 1993. The bars represent the proportion of 39 regular first-response units equipped with automated external defibrillators (AEDs). The AED protocol was modified early in 1994.

changes in the AED protocol were instituted in a noninvestigation setting to correct a failed treatment strategy (Figure 1); accordingly, approval was not requested from an institutional review board.

When a cardiac arrest was suspected, a minimum of 7 persons in 3 units were dispatched. Therapy for cardiac arrest was carried out according to American Heart Association guidelines.¹¹ Cardiopulmonary resuscitation was reinstated for a pulseless state after either delivery of 3 shocks or 2 consecutive analyses without shocks advised. After each use of an AED, routine feedback to the EMTs reinforced the pre-shock CPR protocol. Initial attempts to convert VF always preceded tracheal intubation and administration of drugs, both of which were carried out in virtually all cases. If paramedics reached the patients before, or simultaneously with, the first responding EMTs, manual rhythm recognition and defibrillation were carried out after instituting CPR, which was performed until the device was readied. When EMT responders arrived first, AEDs were applied to individuals with cardiac arrest unless there was livido or rigidity.

The basic data relating to each cardiac arrest included response intervals of EMT and paramedic units, therapy administered, survival status, whether the arrest was witnessed, application of bystander-initiated CPR, and location of the cardiac arrest. Response intervals were calculated from time of dispatch and arrival as reported by a central computer system from which seconds were not transcribed. In this report we considered all patients 18 years or older whose first recorded rhythm was VF and who received advanced cardiac life support including 1 or more defibrillation shocks plus tracheal intubation or establishment of an intravenous line. The total period of observation was from July 1, 1990, to December 31, 1996.

Survival and neurologic status at hospital discharge were obtained from the hospital record as part of the emergency medical services quality improvement program. Hospital records of survivors were made available after receipt of permission from the patient or family. Based on review of the hospital record, experienced abstractors coded patients as having 1 of 4 functional levels at the time of hospital discharge from

Table 1. Patients Treated for Out-of-Hospital Ventricular Fibrillation*

	Preintervention (Immediate Defibrillation) 7/1/90-12/31/93	Intervention Period (90-Second CPR Protocol) 1/1/94-12/31/96	P Value†
Patients, No.	639	478	. . .
Average age, y (SD)	66.5 (14.4)	66.6 (15.1)	.58
Men, %	77.8	75.9	.48
Presumed cardiac etiology, %	97	96	.36
Witnessed arrests, %	73	70.5	.44
Bystander-initiated CPR, %	58.1	57.5	.86
Average response intervals, min (SD)‡			
First arriving unit	3.7 (1.5)	3.6 (1.5)	.16
Paramedic unit	7.5 (4.0)	7.9 (3.6)	.01
AED applied by EMTs, %	72.3	81.4	<.001
Shocked by EMTs, %	68.5	74.2	.04
Simultaneous EMT and paramedic dispatch, %	91.7	85.8	<.002
Race, %			
White	82.8	82.0	.65
Black	10.2	11.7	
Other	7.0	6.3	
Site of arrest, %			
Home	57.7	56.5	.77
Public location§	39.6	40.2	
Extended care facility	2.7	3.3	

*All patients were in cardiac arrest when initially examined, and ventricular fibrillation was the first recorded rhythm. CPR indicates cardiopulmonary resuscitation; AED, automated external defibrillators; EMT, emergency medical technician; and ellipses, not applicable.

†Statistical significance of difference between the 2 ages, proportions, or intervals.

‡From first dispatch to arrival at scene.

§Nonresidential sites (indoors or outdoors) accessible to the public, including physicians' offices and clinics.

an acute care service. Level 1 involved full or nearly full neurologic recovery with apparently intact brain function. Patients may have had minor short-term memory deficits or generalized weakness, but the likelihood for complete neurologic recovery was high. Level 2 patients may have had major memory loss, naming difficulty, coordination deficits, and they may have required assistance with activities of daily living. Such patients were not entirely dependent on others for support. Subsequent functional improvement was anticipated, but the degree uncertain. Level 3 patients were awake with obviously impaired neurologic status. They may have been without language or have required at least short-term supervision because of inability to reason or to follow instructions. The degree of persistent neurologic disability could not be predicted. Level 4 patients were unresponsive and comatose or vegetative.

For 8 patients who did not authorize release of hospital records but who were contacted by telephone, the abstractor assigned 1 of 2 neurologic morbidity categories based on the responses: no apparent impairment or some morbidity with the degree not determined. Patients with level 1 or level 2 function were considered to have had favorable early neurologic recovery; those with level 3 or level 4 function, unfavorable neurologic recovery.

Survival experience and early neurologic recovery were examined in 2 consecutive periods, ie, before and after implementation of a modified AED protocol: July 1, 1990, through December 31, 1993, and January 1, 1994, through December 31, 1996. The beginning date (July 1, 1990) was selected because by then, each of the fire department's 39 regular first-responding units had the training and capability for defibrillation prior to arrival of the paramedics. (An additional 11 ladder companies and

1 fire boat were also equipped with defibrillators, but these units were rarely called on for cases of cardiac arrest.) Because of earlier discussions regarding plans for the change in the AED protocol, some EMTs had begun to adopt the change during the 2 months before dissemination of the protocol. Hence, we chose to consider January 1, 1994, as the beginning date for the intervention.

Prior to analyzing the outcomes, we postulated that any resultant survival benefit would be most evident in cases in which the response intervals of first arriving units were longest, ie, those with greater delay from collapse to delivery of the first shock. For the continuous variables, the *t* test (2-tailed) or the Mann-Whitney rank sum test was used to estimate the significance of differences in means between groups; the χ^2 test and Fisher exact test were used to estimate the significance of differences in 2×2 and other contingency tables. Additional statistical measures included stepwise multivariate logistic regression analysis¹²; such models were considered appropriate after ascertaining that the goodness of fit statistics were nonsignificant.

RESULTS

Patients

All patients were found in cardiac arrest when first examined. Over the 78 months covered in this report, fire department EMTs and paramedics treated 1117 patients aged 18 years or older who had VF as the first recorded cardiac rhythm and had known initial response intervals. This excludes 5 patients younger than 18 years, as well as 5 others whose initial response intervals were unknown. Of the 1117, 97% were considered to have developed cardiac arrest on a cardiac basis. During the months covered in this report, 1602 other adults with nontraumatic cardiac arrest were treated by Seattle Fire Department paramedics in conjunction with EMTs: 936 with asystole, 654 with pulseless electrical activity, and 12 with ventricular tachycardia. These patients are not further considered in this article.

Table 2. Rates of Hospital Admission and Survival According to Response Intervals of the First Arriving Unit*

	Witnessed Cases			All Cases		
	Preintervention Period	Intervention Period	P Value†	Preintervention Period	Intervention Period	P Value†
Patients						
RI <4	229	176		318	258	
RI ≥4	235	161		321	220	
Total	464	337		639	478	
Resuscitated and admitted to hospital						
RI <4	154 (67)	122 (69)	.66	186 (59)	156 (61)	.63
RI ≥4	127 (54)	101 (63)	.09	154 (48)	125 (57)	.04
Total	281 (61)	223 (66)	.10	340 (53)	281 (59)	.06
Discharged alive						
RI <4	85 (37)	72 (41)	.44	99 (31)	82 (32)	.87
RI ≥4	51 (22)	53 (33)	.02	56 (17)	60 (27)	<.007
Total	136 (30)	125 (37)	.02	155 (24)	142 (30)	.04
Discharged with favorable neurologic recovery‡						
RI <4	59 (26)	62 (36)	.04	64 (20)	69 (27)	.06
RI ≥4	38 (16)	37 (23)	.09	42 (13)	40 (18)	.11
Total	97 (21)	99 (30)	<.006	106 (17)	109 (23)	.01

*RI indicates response interval from dispatch until the first arriving vehicle stops at the location of the incident, measured in minutes; all data except P values are given as number or number (percentage).

†Statistical significance of difference between the 2 intervals.

‡Excludes 9 patients with undetermined neurologic status.

The 1117 VF patients are described in TABLE 1: 639 during 42 months before intervention and 478 during the 36 months after intervention. The characteristics and service-related variables were generally similar in the periods. Of note, however, was the greater incidence of cases in the earlier time period (average 183 vs 159 per year) and also the greater rates of AED use during the latter period (72% vs 81%, $P<.001$). The latter difference was associated with somewhat longer paramedic response intervals from EMT dispatch and hence greater opportunity for AED use by the EMTs. Paramedics arrived on the scene before the EMTs in only a small number of cases: 23 (3.6%) in the preintervention period and 13 (2.7%) during the intervention period.

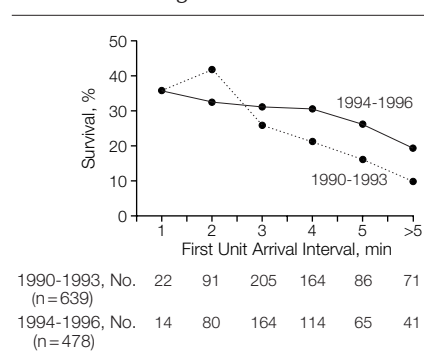
Survival

As shown in TABLE 2, the overall survival rate (to hospital discharge) was greater during the intervention than in the preintervention period: 30% vs 24% ($P = .04$). Similarly, in cases of witnessed cardiac arrest, the survival rates after and before intervention were 37% and 30%, respectively ($P = .02$). When survival was considered

in relation to the response interval of the first arriving unit, it was apparent that the benefit associated with the intervention period occurred mainly in patients whose response intervals were 4 minutes or longer (FIGURE 2, and Table 2).

When survival was analyzed using multivariate logistic regression, the effect of the intervention period remained a significant and independent factor (odds ratio, 1.42; 95% confidence interval, 1.07-1.90; $P = .02$) after adjusting for covariates affecting survival (response intervals, witnessed collapse, bystander-initiated CPR, age, public location). Variables that were not significant included sex, use of AED, shock by first responding EMTs, and race. Significant odds ratios and 95% confidence intervals are displayed in FIGURE 3. An interaction between response interval of the first arriving unit and the study period was also independently significant. The interaction, which was an a priori hypothesis, described a relatively greater survival benefit for CPR before defibrillation as response intervals increased (and as the survival rate decreased), ie, the adjusted odds ratio of the study period was 0.8 for a 1-minute

Figure 2. Survival in the 2 Study Periods According to the Response Intervals of the First Arriving Unit



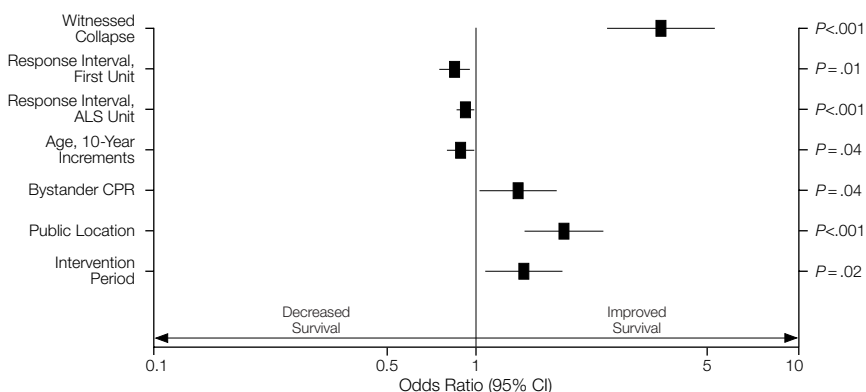
response interval, 2.1 for a 5-minute interval, and 6.8 for a 10-minute interval.

Also shown in Table 2, the rates of hospitalization following successful initial resuscitation tended to be greater in the intervention period—particularly in cases in which the response interval of the first arriving unit was 4 minutes or longer ($P = .04$).

Neurologic Status at Hospital Discharge

An assessment of early neurologic recovery in 297 survivors was deter-

Figure 3. Odds Ratios for Survival: 1117 Cases of Out-of-Hospital Ventricular Fibrillation



The odds ratios (derived from a multivariate logistic regression model) for response intervals are shown for 1-minute differences. ALS indicates advanced life support; CI, confidence interval; and CPR, cardiopulmonary resuscitation. Longer response intervals and greater age were independent predictors of worse survival rates. Significantly improved survival rates were associated with the other variables shown.

Table 3. Patients Discharged Alive*

	Preintervention Period	Intervention Period	P Value
No. of survivors	155	142	...
Treated cases, %	24	30	.04
Mean (SD) hospital stay, d	18.4 (12.8)	13.3 (8.7)	<.001
Median, d	16	11	...
Mean (SD) time to awaken, d†	2.3 (4.1)	1.9 (2.3)	.42
Median, d	1	1	...
No. (percentage) discharged to			
Home	108 (70)	96 (68)	.55
Nursing home	35 (23)	29 (21)	
Rehabilitation center	12 (8)	16 (11)	
Unknown	...	1 (0.7)	
Neurologic function at hospital discharge, No. assessed	150	138	...
Results, No. (%)			
Level 1	92 (61)	92 (67)	.03
Level 2	14 (9)	17 (12)	
Level 3	42 (28)	22 (16)	
Level 4	2 (1)	7 (5)	
Favorable initial outcome (level 1 + level 2)	106 (71)	109 (79)	.11

*Ellipses indicate not applicable. Levels of function are defined in the "Methods" section.
 †For patients who awakened.

mined from the hospital record for 284 patients (96%), by telephone interview for 8 (3%), and was unknown for 5 (2%). Of the 8 survivors with a morbidity status obtained by telephone interview, 4 were reported to have made a full recovery at hospital discharge and 4 were reported to have partial to moderate disability. These latter 4 and the 5 unknowns were not included in the analysis of neurologic recovery because their neurologic outcome could

not be classified as favorable or unfavorable. Five of the 9 were from the early period, and 4 were from the intervention period.

Accordingly, 288 survivors were classified into 2 groups for analysis of factors contributing to morbidity level among survivors. The first group (favorable early outcomes) consisted of the 215 patients considered to have level 1 (n = 184) or level 2 (n = 31) neurologic function. A second group (unfa-

vorable early outcomes) consisted of 73 patients who were confirmed by hospital record to have been discharged with level 3 (n = 64) or level 4 (n = 9) function.

Estimates of early neurologic outcomes are summarized in Table 2 and TABLE 3. Surviving patients who had been treated during the intervention period had a greater, but nonsignificant, incidence of favorable outcomes compared with those in the preintervention period (79% vs 71%; P = .11). The improved early neurologic recovery was evident only in cases with initial response intervals of less than 4 minutes (87% vs 67%; P < .002). However, a relationship between better neurologic outcome in the shorter response intervals was not an a priori hypothesis. Overall, the proportion of treated victims who were discharged alive and with favorable neurologic outcomes was significantly increased during the intervention period (106/634 [17%] vs 109/474 [23%], P = .01; Table 2).

COMMENT

Certainly defibrillation is a sine qua non for the effective treatment of VF. But it is also clear that defibrillation alone by no means ensures survival, restoration of circulation, or even establishment of an organized cardiac rhythm, particularly when there have been delays in initiating treatment, as typically occurs with cardiac arrest outside the hospital. In the early years of prehospital emergency care, defibrillation was provided only by paramedic teams, often with considerable delays in response intervals. However, the provision of CPR by bystanders or earlier arriving rescue personnel appeared to compensate, at least to some extent, for the unavoidable delays in defibrillation.^{1,2}

The principal finding in this report is that the survival of patients treated for out-of-hospital VF during 1994 through 1996 was significantly improved over comparable patients who were treated during the preceding 42 months—most evident in cases in which the first responding unit arrived 4 minutes or longer after dispatch. While the proto-

col for EMT defibrillation was clearly changed in the later period to require CPR prior to the delivery of the initial shock, we cannot definitely exclude other bases for the increased survival rate, eg, spontaneous improvement or an undetected difference in the characteristics of the patients. However, neither of these possibilities seems likely in view of the relatively stable, or even declining, survival rates that had occurred over the several years preceding the change in AED/CPR policy (Figure 1). An additional factor that could have had a confounding influence is that of a concurrent pharmacologic trial during the latter 25 months covered in this report. From December 1994 through February 1997 a randomized trial of amiodarone vs placebo was conducted in a subset of patients with resistant or recurrent VF. However, in that trial only 16% of patients in the intervention period received amiodarone (9% of survivors); additionally, amiodarone showed no significant survival benefit.¹³ Hence, we believe it unlikely that the amiodarone trial influenced the findings reported here.

The number of cases was lower in the latter time period of this study. A local trend for declining cases of VF over time has been noted previously,⁹ and is likely related to the continued nationwide reduction of age-adjusted mortality attributed to coronary heart disease.¹⁴ It is appropriate to emphasize that the patients studied in this report represent a population-based cohort in a city in which there is a single emergency medical services system.

The improvement in survival during the intervention period was predominantly in patients for whom the response interval was 4 minutes or longer. This time-related effect was postulated a priori, based on the high likelihood of a good outcome when advanced life support is provided within a minute or two after the development of VF.^{3,15} Additionally, we were influenced by the experimental evidence of Niemann and colleagues⁸ demonstrating in dogs that resuscitation initiated after 7.5 minutes of VF was substantially more effective fol-

lowing pretreatment with CPR and epinephrine compared with immediate defibrillation.

The provision of CPR prior to delivery of a precordial shock for VF is not novel. For a number of years it was considered useful to apply CPR to "coarsen VF"; however, that policy has largely been abandoned in favor of defibrillation as soon as possible for virtually all patients with VF.^{16,17} Clearly, immediate defibrillation for monitored patients who develop VF (or ventricular tachycardia) is highly effective when patients are treated within a minute or thereabouts; such patients have excellent outcomes as shown by many years of experience in coronary care units and in other situations in which defibrillators are immediately available. However, those experiences do not apply to situations in which there has been several minutes' delay before delivery of a shock. Typically, VF can be converted, but the resultant rhythm is often asystole or pulseless electrical activity resistant to further treatment. The basis for the worsened electrical and mechanical cardiac function with prolonged VF seems to be related to the relatively high metabolic requirements for VF, loss of oxygen delivery, and the ultimate depletion of metabolic substrates and high-energy phosphate stores.^{18,19} There is evidence suggesting that the myocardial metabolic degradation may be slowed or partially reversed by CPR.^{19,20}

As noted above, a major question is whether the improved survival reported here can be attributed to a change in the AED protocol. We believe that our observations represent an encouraging pilot study and that the development of randomized clinical trials be considered to evaluate further the influence of CPR before the delivery of a shock for patients who have had significant delay prior to treatment. We also point out that the 90-second period of CPR in this report was arbitrarily chosen and that studies might address the optimal duration for CPR prior to shock. Although a precise measurement is not available, we estimate that

the greater emphasis on CPR in the intervention period delayed the delivery of a shock by something less than the full 90 seconds, ie, CPR appears to have been more efficiently initiated. It should be noted that in earlier years, prior to the institution of defibrillation by EMTs, relatively good survival rates were achieved under conditions in which CPR was provided an average of 5 minutes before paramedics arrived (Figure 1).⁶ There is an awareness that early defibrillation for patients with VF is a critical element for successful resuscitation. In general that is undoubtedly correct, but the observations reported here suggest that this association may not pertain under all conditions. Conceivably, it might be possible to improve outcomes by individualizing therapy according to delays already incurred and perhaps to the characteristics of the VF waveform.²¹

An important facet of our experience with EMT defibrillation is the fact that survival overall had not improved with the addition of that procedure—in fact, there is some suggestion that survival rates had trended downward (Figure 1). Other communities have reported either small, non-significant survival benefit²² or no apparent improvement²³⁻²⁶ after EMT defibrillation had been incorporated into 2-tiered urban emergency medical services systems.

Additionally, we call attention to the probably detrimental effect of EMT defibrillation protocols for patients with asystole or pulseless electrical activity. Although survival for the former condition is dismal under almost any condition, a modest proportion of patients with pulseless electrical activity can be expected to survive. For such patients, attention directed to the use of AEDs and away from CPR would seem to be disadvantageous—another reason for the provision of at least a brief period of CPR before proceeding with the use of an AED.

We observed a trend for improved early neurologic recovery during the intervention period (Tables 2 and 3), and indeed, enhanced brain perfusion could

have contributed substantially to the survival benefit with CPR. A potential confounding element for the estimate of neurologic recovery was the timing of the assessment at hospital discharge. The median hospital stay for survivors was 5 days shorter during the intervention period, a fact undoubtedly influenced by the prevailing economic concern to reduce hospital stay.

Whatever the reasons for earlier discharge, the opportunity to observe improvement²⁷ was abbreviated, thereby allowing a possible underestimation of neurologic recovery in patients treated during the intervention period.

In summary, our findings support previous experimental work suggesting that CPR prior to defibrillation is of benefit when there has been several

minutes' delay before a shock can be delivered to patients with out-of-hospital VF.

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