

# Delaying Defibrillation to Give Basic Cardiopulmonary Resuscitation to Patients With Out-of-Hospital Ventricular Fibrillation

## A Randomized Trial

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**E**ARLY DEFIBRILLATION IS CRITICAL for survival from ventricular fibrillation. The survival rate decreases by 3% to 4% or 6% to 10% per minute depending on whether basic cardiopulmonary resuscitation (CPR) is performed.<sup>1,2</sup> Another major factor known to influence survival in patients with ventricular fibrillation is whether CPR is performed prior to when a defibrillator is available.<sup>1</sup> It has been assumed that the blood flow generated by CPR decreases the rate of deterioration of the heart and brain cells,<sup>3</sup> but is insufficient to improve the state of the tissues. If tissue perfusion could be improved, withholding defibrillation for a short period while administering CPR might improve the results for patients with depleted myocardial levels of high-energy phosphates,<sup>3</sup> severe acidosis,<sup>4</sup> and a ventricular fibrillation frequency spectrum indicating a low chance of defibrillation success.<sup>3,6</sup>

In an experimental study, defibrillation was more successful following basic CPR and high-dose epinephrine than immediate defibrillation in dogs with

**Context** Defibrillation as soon as possible is standard treatment for patients with ventricular fibrillation. A nonrandomized study indicates that after a few minutes of ventricular fibrillation, delaying defibrillation to give cardiopulmonary resuscitation (CPR) first might improve the outcome.

**Objective** To determine the effects of CPR before defibrillation on outcome in patients with ventricular fibrillation and with response times either up to or longer than 5 minutes.

**Design, Setting, and Patients** Randomized trial of 200 patients with out-of-hospital ventricular fibrillation in Oslo, Norway, between June 1998 and May 2001. Patients received either standard care with immediate defibrillation (n=96) or CPR first with 3 minutes of basic CPR by ambulance personnel prior to defibrillation (n=104). If initial defibrillation was unsuccessful, the standard group received 1 minute of CPR before additional defibrillation attempts compared with 3 minutes in the CPR first group.

**Main Outcome Measure** Primary end point was survival to hospital discharge. Secondary end points were hospital admission with return of spontaneous circulation (ROSC), 1-year survival, and neurological outcome. A prespecified analysis examined subgroups with response times either up to or longer than 5 minutes.

**Results** In the standard group, 14 (15%) of 96 patients survived to hospital discharge vs 23 (22%) of 104 in the CPR first group ( $P=.17$ ). There were no differences in ROSC rates between the standard group (56% [58/104]) and the CPR first group (46% [44/96];  $P=.16$ ); or in 1-year survival (20% [21/104] and 15% [14/96], respectively;  $P=.30$ ). In subgroup analysis for patients with ambulance response times of either up to 5 minutes or shorter, there were no differences in any outcome variables between the CPR first group (n=40) and the standard group (n=41). For patients with response intervals of longer than 5 minutes, more patients achieved ROSC in the CPR first group (58% [37/64]) compared with the standard group (38% [21/55]; odds ratio [OR], 2.22; 95% confidence interval [CI], 1.06-4.63;  $P=.04$ ); survival to hospital discharge (22% [14/64] vs 4% [2/55]; OR, 7.42; 95% CI, 1.61-34.3;  $P=.006$ ); and 1-year survival (20% [13/64] vs 4% [2/55]; OR, 6.76; 95% CI, 1.42-31.4;  $P=.01$ ). Thirty-three (89%) of 37 patients who survived to hospital discharge had no or minor reductions in neurological status with no difference between the groups.

**Conclusions** Compared with standard care for ventricular fibrillation, CPR first prior to defibrillation offered no advantage in improving outcomes for this entire study population or for patients with ambulance response times shorter than 5 minutes. However, the patients with ventricular fibrillation and ambulance response intervals longer than 5 minutes had better outcomes with CPR first before defibrillation was attempted. These results require confirmation in additional randomized trials.

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7.5 minutes of untreated ventricular fibrillation.<sup>7</sup> In a nonrandomized human study, Cobb et al<sup>8</sup> reported that 90 seconds of CPR by ambulance personnel before defibrillation improved survival to hospital discharge compared with a historic control group. We therefore designed this clinical trial to determine whether CPR prior to defibrillation (CPR first) would improve outcomes in patients with out-of-hospital ventricular fibrillation.

## METHODS

### Study Design

The Regional Committee for Medical Research Ethics, which is an independent but nationally coordinated committee of members who are appointed by the Minister of Education, Research, and Church Affairs based on recommendations from the Research Council of Norway, approved the study protocol. Informed consent for inclusion in the study was waived as decided by this committee in accordance with paragraph 26 in the Helsinki Declaration,<sup>9</sup> but was required for including 1-year follow-up data.

The study was conducted in the Oslo emergency medical service (EMS) system, which covers a land area of 427 km<sup>2</sup> and a population of approximately 500 000. Of this population, 48% were men and 16% were older than 65 years. The study was a randomized, controlled trial involving patients older than 18 years with ventricular fibrillation or pulseless ventricular tachycardia in whom the ambulance personnel had not witnessed the cardiac arrest. On-site randomization after defibrillator electrocardiogram verification of ventricular fibrillation/ventricular tachycardia was performed by opening a sealed study envelope that contained the treatment assignment. The ambulance personnel could not be blinded thereafter. Hospital personnel were blinded, including the physicians responsible for assessing the neurological outcome at hospital discharge. The study was monitored by a physician not involved in the care of any patients or in data collection. This physician received all case records and the sealed randomization list after 6, 18, and

30 months, and performed interim analyses of outcome. If significant differences in survival were detected ( $P < .05$ ), the study would have been stopped. Subgroups of patients with response times either up to or longer than 5 minutes were also included in the monitoring.

### Treatment Protocol

The patients were attended by either 1 ambulance with an anesthesiologist and 2 paramedics, or 2 ambulances with 2 ambulance personnel each and a minimum of 1 paramedic per ambulance. The equipment, drugs, and procedures were identical on all units including the physician-staffed unit. Advanced cardiac life support was provided according to the guidelines of the European Resuscitation Council<sup>10</sup> except for the duration of CPR (defined as chest compressions and ventilation) prior to a defibrillation attempt, which was the intervention studied. When the ambulance arrived, a monophasic automated defibrillator (LIFEPAK 12, Medtronic Physio-Control, Redmond, Wash) was immediately applied to the patient by 1 EMS staff member and all patients with ventricular fibrillation/pulseless ventricular tachycardia were included. The other rescuer intubated the patient as soon as possible without disturbing the electrocardiographic analysis.

In the standard group, a defibrillating shock of 200 J was given immediately. If unsuccessful, defibrillation was repeated once with 200 J, and if necessary once more with 360 J. If return of spontaneous circulation (ROSC) was not achieved, 1 minute of CPR was given for ventricular fibrillation/ventricular tachycardia or 3 minutes for nonventricular fibrillation/ventricular tachycardia before a new rhythm analysis and the shock and CPR sequence was repeated as indicated with all shocks at 360 J. All patients were ventilated with 100% oxygen and given 1 mg of epinephrine intravenously every 3 minutes until ROSC or termination of the resuscitation attempt. Epinephrine should be administered in the beginning of a chest compression-ventilation interval, and was therefore

not given before the first defibrillation attempt in either group due to the time required before an intravenous line with a continuous drip of 500 mL of Ringer acetate could be established.

The CPR first group was treated identically except that CPR was given for 3 minutes prior to the first defibrillation attempt, and if CPR was needed thereafter, it was given for 3 minutes both for ventricular fibrillation/ventricular tachycardia and nonventricular fibrillation/ventricular tachycardia. Countershock refractory ventricular fibrillation or recurrent ventricular fibrillation was treated according to the 1998 European Resuscitation Council guidelines.<sup>10</sup> A standard 100-mg dose of lidocaine was given intravenously only after 9 defibrillation attempts. Other antiarrhythmics, such as amiodarone, were not given.

### Data Collection

Data were collected according to the Utstein style.<sup>11</sup> Out-of-hospital data were based on the digital dispatcher database, the ambulance records, and the Utstein data collection sheets. These data included the therapy administered, whether the cardiac arrest was witnessed, application of bystander-initiated CPR, location of the cardiac arrest, and response-time intervals calculated from time of dispatch of the first ambulance to arrival of the first ambulance as registered on-line by a central computer system in the dispatch center. A computer board and screen in the ambulance were connected to this central computer, and enabled the ambulance personnel to log the time of arrival directly on this computer, which was the same one that dispatched the ambulance, thus avoiding a time synchronization problem. The time of patient collapse was estimated by the ambulance personnel based on the information they received from bystanders, and manually synchronized with the time on the computer screen. Time intervals from arrival at the patient's location until direct current shock and ROSC were taken from the defibrillator and did not need to be synchronized with the other time points.

Survival and neurological status at hospital discharge were obtained from the hospital record. Neurological status was assessed according to the Glasgow-Pittsburgh outcomes, which consist of the cerebral performance category (CPC) and the overall performance category (OPC) with CPC/OPC of 1 indicating a good cerebral/good overall performance; CPC/OPC of 2, moderate cerebral/moderate overall disability; CPC/OPC of 3, severe cerebral/severe overall disability; CPC/OPC of 4, coma/vegetative state; and CPC/OPC of 5, brain death/death.<sup>12</sup> One-year follow-up data were collected from a questionnaire (available from the authors on request) sent to patients or their relatives during May 2002.

All data were stored in a database (FileMaker Pro, Version 4.1, FileMaker Inc, Santa Clara, Calif) and analyzed using an SPSS statistical package (Version 11.0, SPSS Inc, Chicago, Ill).

### Outcomes

The primary outcome was survival to hospital discharge. Secondary outcomes were ROSC and survival to hospital, overall status scored as OPC and neurological status scored as CPC at discharge, and 1-year survival with neurological status.

### Statistical Analysis

Prior to analyzing the outcomes, we postulated that any resultant survival benefit would be most evident in cases with longer response intervals based on the report by Cobb et al,<sup>8</sup> which was published while our study was still ongoing. We decided prior to data analysis to analyze subgroups with response times either up to or longer than 5 minutes.<sup>13,14</sup> Cobb et al<sup>8</sup> used a response interval of 4 minutes. These response times are longer than those used in Seattle,<sup>8</sup> and we expected that we would have too few patients in a group with response intervals shorter than 4 minutes. This decision was made by the 2 main authors (L.W. and P.A.S.) alone and communicated to the other authors, but not to any other personnel involved in the study.

A power analysis using Sigmasat statistical software (Version 2.03, SPSS Inc) provided a power of 80 for  $\alpha$  of .05 with 250 patients in each group for an increased survival from 15% for the standard group to 25% for the CPR first group. The survival of ventricular fibrillation patients has been 16% to 18% in previous studies of standard advanced cardiac life support in this EMS system.<sup>13,14</sup>

Categorical data were analyzed by the  $\chi^2$  (alternatively the Fisher-Irwin) test and numerical data by the Mann-Whitney U test. We calculated the odds ratios (ORs) and 95% confidence intervals (CIs) using SPSS statistical software.  $P < .05$  was considered significant.

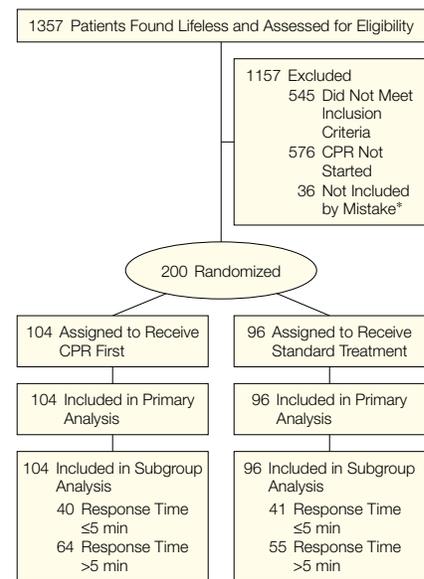
To assess differences between the standard treatment and the CPR first groups, a logistic regression analysis was performed. The dependent variable of discharged alive was regressed on the independent variables of group, age, sex, whether cardiac arrest was witnessed, whether CPR was performed by a bystander, location of cardiac arrest, and response time interval. The interaction term between group and response time interval was also included. This term represents differences between the standard and the CPR first groups, with respect to probability of survival to hospital discharge as a function of response time, and it may specifically be used to test the hypothesis generated by Cobb et al<sup>8</sup> that a CPR first strategy only benefits patients with longer response times.

## RESULTS

### Study Population

Between June 1998 and May 2001, 1357 patients were found lifeless and advanced CPR was started on 781 patients; 466 had asystole and 55 had pulseless electrical activity. Of 260 cardiac arrests with ventricular fibrillation as the first documented rhythm, 24 were witnessed by EMS personnel and were therefore excluded. The randomization envelope was missing in 2 cases. Thirty-four patients were not included in the study because EMS personnel failed to enroll them even though they met study criteria (FIGURE 1).

**Figure 1.** Flow Diagram of CPR First and Standard Care



CPR indicates cardiopulmonary resuscitation. Asterisk indicates emergency medical service personnel failed to enroll patients even though they met study criteria; the randomization envelope was missing for 2 patients.

The baseline characteristics of the 200 patients included in the study are shown in TABLE 1. There were no significant differences between the study groups in terms of age, sex, EMS response times, location of the cardiac arrest, proportion of cardiac arrests that were witnessed, or times CPR was performed by a bystander. The physician-manned ambulance was dispatched to 25 (24%) of 104 patients in the CPR first group and to 22 (23%) of 96 patients in the standard treatment group. There was no difference in the use of epinephrine or lidocaine in the 2 groups.

### Outcome

There was no difference between the CPR first group and the standard group in the survival rate to hospital discharge (22% [23/104] vs 15% [14/96];  $P = .17$ ); ROSC rates (56% [58/104] vs 46% [44/96];  $P = .16$ ); or 1-year survival (20% [21/104] vs 15% [14/96];  $P = .30$ ) (TABLE 2). Of 37 patients discharged alive, 33 (89%) were re-

ported to have made a good neurological recovery at hospital discharge (CPC/OPC of 1 or 2) with no difference between the groups at discharge or when evaluated by the patient or a relative 1 year after cardiac arrest (TABLE 3). As of May 2002, 29 patients were still alive and 27 patients or their relatives responded to the fol-

low-up survey. Two patients did not respond (1 patient in each group; both had been in the interval of  $\leq 5$  minutes).

For the 81 patients with ambulance response times of 5 minutes or less, there were no differences in ROSC, survival to hospital discharge, 1-year survival, or neurological outcome of survivors (Table 2 and Table 3).

For the 119 patients with response times longer than 5 minutes, more patients in the CPR first group than in the standard group achieved ROSC (58% [37/64] vs 38% [21/55];  $P = .04$ ); survival to hospital discharge (22% [14/64] vs 4% [2/55];  $P = .006$ ); and 1-year survival (20% [13/64] vs 4% [2/55];  $P = .01$ ) (Table 2).

In logistic regression analysis, both forward and backward stepwise variable selection procedures resulted in a model with the predictor variables of age (OR, 0.97; 95% CI, 0.94-0.99), CPR performed by a bystander (OR, 3.75; 95% CI, 1.49-9.42), response time (OR, 0.68; 95% CI, 0.52-0.90), and the interaction term between group and response time present (OR, 1.41; 95% CI, 1.03-1.94).

Specifically, the interaction term is significant ( $P = .03$ ). The term group is also included since it is involved in a significant interaction. Leaving it out implies only minor differences in the results. FIGURE 2 shows the estimated probability of survival to hospital discharge plotted against response time. The significant interactions between group and response time means that the shapes of the curves are significantly different. The estimated survival with CPR first vs standard therapy is a function of the response time interval formula ( $-1.305 + 0.346 \times \text{Time}$ ), indicating a higher chance of survival with CPR first for response time intervals longer than 4 minutes.

The calculated OR for survival with CPR before defibrillation increased from 0.4 (95% CI, 0.08-1.80) for a less than 1-minute response interval to 3 (95% CI, 1.06-8.79) for a 7-minute interval, and 6.1 (95% CI, 1.34-27.80) for a 9-minute interval.

## COMMENT

In this study, there were no overall differences in survival for patients with out-of-hospital ventricular fibrillation who received standard care vs CPR first prior to defibrillation. However, for patients with longer ambulance response times ( $> 5$  minutes), the hospital discharge and 1-year survival rates were higher for patients who had re-

**Table 1.** Baseline Characteristics of Patients

Characteristic	No. (%)		P Value
	CPR First (n = 104)	Standard (n = 96)	
Age, median (range), y	71 (18-88)	70 (18-96)	.57
Men	88 (85)	85 (89)	.42
Cardiac arrest observed by others	95 (91)	90 (94)	.52
Bystander performed CPR	64 (62)	54 (56)	.41
Location of cardiac arrest			
Home	51 (49)	42 (44)	.39
Public place	36 (35)	42 (44)	
Other	17 (16)	12 (12)	
Time, mean (95% CI), min			
Collapse to ambulance arrival	12.0 (10.7-13.4)	11.7 (10.7-12.7)	.76
Arrival to first defibrillation attempt	3.8 (3.4-4.2)	1.9 (1.6-2.2)	<.01
First defibrillation attempt to ROSC	12.9 (9.2-16.5)	14.4 (11.5-17.3)	.22
Collapse to ROSC	26.9 (23.4-30.4)	26.7 (23.6-29.8)	.74
Dose of epinephrine, mean (95% CI), mg	5.3 (4.3-6.4)	5.0 (4.2-5.9)	.74
Lidocaine given intravenously	22 (21)	21 (22)	>.99

Abbreviations: CI, confidence interval; CPR, cardiopulmonary resuscitation; ROSC, restoration of spontaneous circulation.

**Table 2.** Rates of Discharge From Hospital, ROSC, and 1-Year Survival\*

Group	No. (%)		OR (95% CI)†	P Value‡
	CPR First (n = 104)	Standard (n = 96)		
	Total			
Discharged from hospital	23 (22)	14 (15)	1.66 (0.80-3.46)	.20
ROSC	58 (56)	44 (46)	1.49 (0.85-2.60)	.20
1-Year survival	21 (20)	14 (15)	1.48 (0.71-3.11)	.35
	$\leq 5$ min			
	(n = 64)	(n = 55)		
Discharged from hospital	9 (23)	12 (29)	0.70 (0.26-1.91)	.61
ROSC	21 (52)	23 (56)	0.87 (0.36-2.08)	.82
1-Year survival	8 (20)	12 (29)	0.60 (0.22-1.69)	.44
	$> 5$ min			
	(n = 40)	(n = 41)		
Discharged from hospital	14 (22)	2 (4)	7.42 (1.61-34.3)	.006
ROSC	37 (58)	21 (38)	2.22 (1.06-4.63)	.04
1-Year survival	13 (20)	2 (4)	6.76 (1.42-31.4)	.01

Abbreviations: CI, confidence interval; CPR, cardiopulmonary resuscitation; OR, odds ratio; ROSC, return of spontaneous circulation.

\*Patients received ventricular fibrillation posthospitalization and 3 minutes of CPR before defibrillation vs standard treatment with immediate defibrillation.

†ORs and 95% CIs were calculated by logistic regression.

‡Calculated from the Fisher exact test.

**Table 3.** Overall Performance Categories and Cerebral Performance Categories of Patients at Hospital Discharge and at 1-Year Survival

Outcome	No. Received Treatment, All Patients				No. Received Treatment, ≤5 min				No. Received Treatment, >5 min			
	CPR First (n = 104)		Standard (n = 96)		CPR First (n = 40)		Standard (n = 41)		CPR First (n = 64)		Standard (n = 55)	
	At Discharge	1 Year	At Discharge	1 Year	At Discharge	1 Year*	At Discharge	1 Year	At Discharge	1 Year	At Discharge	1 Year
Overall performance category												
1	11	8	9	9	3	2	7	7	8	6	2	2
2	9	7	4	3	4	2	4	3	5	5	0	0
3	1	0	1	0	0	0	1	0	1	0	0	0
4	2	0	0	0	2	0	0	0	0	0	0	0
5 (Dead)	81	82	82	82	31	32	29	29	50	50	53	53
Unknown*	0	7	0	2	0	4	0	2	0	3	0	0
Cerebral performance category												
1	14	6	7	7	4	3	5	5	10	3	2	2
2	6	9	4	4	3	1	4	4	3	8	0	0
3	1	0	1	1	0	0	1	1	1	0	0	0
4	2	0	0	0	2	0	0	0	0	0	0	0
5 (Dead)	81	83	82	83	31	33	29	30	50	50	53	53
Unknown*	0	6	2	1	0	3	2	1	0	3	0	0

Abbreviation: CPR, cardiopulmonary resuscitation.

\*There are no differences between the groups when comparing patients surviving (overall performance category and cerebral performance category 1 through 4) to either hospital discharge or 1 year after cardiac arrest. In both the CPR first and the standard treatment group, 1 patient with response time of 5 minutes or less failed to answer the questionnaire. The other patients with unknown scores lived longer than 1 year, but died before the questionnaire was sent out in May 2002.

ceived 3 minutes of CPR prior to defibrillation and then 3-minute intervals of CPR (instead of 1 minute) between defibrillation attempts. This finding is in agreement with Cobb et al<sup>8</sup> who found 27% survival to hospital discharge with 90 seconds predefibrillation CPR vs 17% in a historic control group without predefibrillation CPR for response times of 4 minutes or longer.

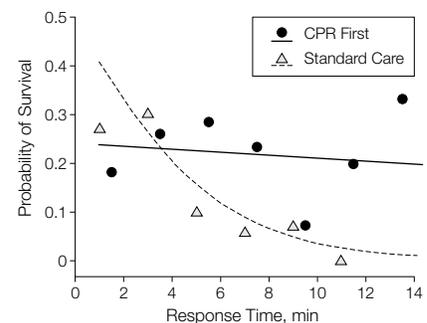
The hospital admission rate of 46% and discharge rate of 15% in the standard group in our study are similar to previously reported results for patients with ventricular fibrillation of 39% to 47% and 16% to 18% even in retrospective studies from this same EMS system.<sup>13,14</sup> When considering these rates along with the fact that cardiac arrest results continuously receive specific focus in this EMS system, we believe a Hawthorne effect (important in prospective clinical research<sup>15</sup>) is unlikely to specifically affect the results in our study.

Robinson et al<sup>16</sup> reported ROSC in 16% of unwitnessed out-of-hospital cardiac arrests with a 4% overall survival rate to hospital discharge. All patients were given CPR for at least 2 minutes prior to first shock, and the principle

of defibrillation first was questioned as these investigators found their survival rate compared favorably with reports from systems using the defibrillation first strategy.

Some experimental studies of ventricular fibrillation demonstrate that CPR increases the defibrillation success rate.<sup>7,17,18</sup> In dogs with 7.5 minutes of initially untreated ventricular fibrillation, the defibrillation success was higher after predefibrillation CPR and high-dose epinephrine than after immediate defibrillation.<sup>7</sup> The same laboratory later reported better results with immediate defibrillation than CPR first in swine with 5 minutes of initially untreated ventricular fibrillation.<sup>19</sup> In a study of dogs, immediate defibrillation was effective for episodes of fibrillation if it was limited to approximately 3 minutes.<sup>17</sup>

There may be a cut-off time also in patients below which defibrillation first is best. Immediate defibrillation is highly effective in monitored patients treated within the first minute or two.<sup>1,20,21</sup> 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.<sup>22</sup>

**Figure 2.** Estimated Probability of Survival to Hospital Discharge Plotted Against Response Time

Average fraction of surviving patients for each 2-minute interval. Lines indicate logistic regression models with time as independent variable fitted separately for each of the 2 groups.

Similar to the results of Cobb et al,<sup>8</sup> we did not find a higher survival rate with CPR prior to defibrillation for patients with short response times, but nor was survival worse. We cannot exclude that this could be due to a type II error, and a much larger study with a finer division of the response times may give better survival with immediate defibrillation for short response times. The best average cut-off time for CPR first vs de-

fibrillation first is therefore not presently known. From our calculations based on this limited material, we hypothesized this to be around a 4- to 5-minute response time.

There did not appear to be a difference in outcome in the CPR first group between patients with response times either up to or longer than 5 minutes. The probability of being discharged alive tended to decrease with time when estimated in a logistic regression model (Figure 2), but the fall-off rate with time before defibrillation was much more apparent in the standard group, which is consistent with previously suggested rates.<sup>2</sup> However, even though the 5-minute cut point was prespecified in this study, the findings are based on non-randomized subgroups, and therefore require confirmation in future clinical trials.

There is no contrast between our study and studies concluding that time to defibrillation is the most important factor for survival.<sup>1,23,24</sup> In those studies, defibrillation was attempted as soon as possible, while deliberately delaying defibrillation to provide CPR was not evaluated. Also, the response time in the present study and thus the time before defibrillation was an important factor for survival, but the analysis indicates that there was an interaction between time and whether the ambulance personnel performed defibrillation prior to CPR. The delay before defibrillation is still important. The outcome from ventricular fibrillation is better with response times of 3 minutes than of 7 or 10 minutes. For response times longer than 5 minutes, the outcomes appear to improve if defibrillation is delayed to perform CPR first. Other evidence from both clinical and animal studies suggests that electroshock of prolonged ventricular fibrillation commonly is unsuccessful,<sup>17</sup> with an increased probability of converting ventricular fibrillation to a more resuscitation-refractory rhythm, such as asystole or pulseless electrical activity.<sup>17</sup>

The basis for the worsened electrical and mechanical cardiac function with prolonged ventricular fibrillation<sup>6</sup> seems related to the relatively high metabolic requirements for ventricu-

lar fibrillation, lack of oxygen supply, and an ultimate depletion of metabolic substrates and high-energy phosphate stores.<sup>3</sup> Cardiopulmonary resuscitation might provide a critical amount of cardiac perfusion and improve the metabolic state of the myocytes in patients with ventricular fibrillation, with a potentially more favorable response to defibrillation.

In our study, defibrillation prior to CPR by the ambulance personnel had an effect on outcomes, even though more than half the patients had received CPR performed by a bystander, which also was associated with survival. Previous studies have indicated that the effects of CPR performed by a bystander depends on the quality.<sup>25</sup> In a study from Oslo,<sup>13</sup> only 47% of the CPR performed by a bystander was rated as good.

Cobb et al<sup>8</sup> used 1.5 minutes of CPR, Robinson et al<sup>16</sup> used 2 minutes, and we used 3 minutes of CPR before defibrillation. The optimal duration of delaying defibrillation to perform CPR may be difficult to define, and most likely depends on the condition of the myocardium, which is dependent on the duration of the cardiac arrest and the quality of CPR performed by a bystander. Ideally, whether CPR should be started and defibrillation postponed should be determined by the frequency spectrum of the electrocardiogram, which can predict the probability of ROSC after defibrillation.<sup>5</sup>

In this study, we also increased the duration of CPR between defibrillation series from 1 to 3 minutes. The probability of ROSC after defibrillation as judged from spectral analysis of the electrocardiogram appears to deteriorate rapidly in the absence of CPR.<sup>6</sup> In patients with a median probability of ROSC of 50%, there was a decrease to a median of 8% after 20 seconds without CPR.<sup>6</sup> A series of 3 defibrillation attempts usually takes approximately 45 seconds, and it was hypothesized that 3 minutes of CPR might be more appropriate than the traditional 1 minute if the myocardium can be improved with CPR.

In this study, the neurological outcome was good in survivors in both

groups. The concern that a strategy that results in a higher rate of ROSC after longer periods of cardiac arrest would generate more survivors with severe neurological damage did not occur. There was no difference in neurological outcome in the patients who survived in the 2 groups, and the results compare favorably with previous research.<sup>8,26</sup> In the study by Cobb et al,<sup>8</sup> there was a tendency toward improved neurological outcome ( $P < .11$ ) in the group who received defibrillation prior to CPR.

Use of the Glasgow-Pittsburgh outcomes (CPC and OPC) is recommended in the international Utstein guidelines for reporting results after cardiac arrest.<sup>11</sup> Most outcome studies only report CPC and OPC at the time of hospital discharge, and the accuracy of this for predicting the function and quality of life later after discharge has been challenged by Hsu et al,<sup>27</sup> who reported that a CPC score of 1 at hospital discharge had a sensitivity of 78% and a specificity of 43% for predicting that quality of life at a later date was the same as or better than prior to cardiac arrest. They also found poor correlation between the CPC and a functional status questionnaire, and stated that part of problem might be caused by the CPC and OPC being scored by physicians and not patients, and that physicians appear to be inaccurate judges of patient function.<sup>27</sup> In the present study, we are reporting 1-year follow-up and the basis of the scores is the patient or relative's own evaluation of function, mood, and memory compared with abilities prior to cardiac arrest. In May 2002 when the follow-up questionnaire was sent out, 29 patients were still alive. Twenty-seven patients or their relatives answered the follow-up questionnaire. With a response rate of 93%, we believe it is unlikely that this can have created much of a bias in the results.

In most cardiac arrest studies, the time intervals from patient collapse are only estimates, but probably are fairly reasonable estimates in our study because 93% were witnessed. This high percentage of cardiac arrests that were witnessed probably explains why this was not an independent predictor of sur-

vival in this study. The high proportion of men in our study (87%) is somewhat higher than previously reported in the same EMS service (76%)<sup>28</sup> or that reported in a large Swedish study with 10966 patients (72%).<sup>29</sup> We have no specific explanation—it could be due to chance.

While defibrillation is the essential intervention in ventricular fibrillation, defibrillation alone does not ensure return of an organized cardiac rhythm, restoration of circulation, or long-term survival, particularly when the start of treatment has been delayed. Providing CPR prior to delivery of a precordial shock for ventricular fibrillation is not novel. For a number of years it was considered useful to apply CPR to “coarsen ventricular fibrillation.” However, that policy was abandoned in favor of defibrillation as soon as possible for all patients with ventricular fibrillation.<sup>30,31</sup> Lack of improvement in survival rate and outcome after sudden cardiac arrest de-

spite global, systematic implementation of current resuscitation guidelines, and based on the study by Cobb et al<sup>8</sup> and our data, signal the need for reevaluation of the recommendations. Weisfeldt and Becker<sup>32</sup> have recently proposed a 3-phase time-sensitive model for treatment of ventricular fibrillation. An approximately 4-minute electric phase with immediate defibrillation, followed by a circulatory phase from approximately 4 to 10 minutes with CPR prior to defibrillation, and a third metabolic phase when circulating metabolic factors, can cause additional injury beyond the factors of the local ischemia.

In summary, our findings support previous experimental and clinical work suggesting that CPR prior to defibrillation may be of benefit when there has been several minutes' delay before defibrillation can be delivered to patients with out-of-hospital ventricular fibrillation. Further trials are needed to evaluate this resuscitation strategy and to de-

termine the optimal duration of CPR first in patients with ventricular fibrillation.

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