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Three-Phase Model of Cardiac Arrest: Time-Dependent Benefit of Bystander Cardiopulmonary Resuscitation

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Evidence has suggested that the pathophysiology of ventricular fibrillation cardiac arrest may consist of 3 time-sensitive phases: electrical, circulatory, and metabolic. We performed a retrospective cohort study of adults in a metropolitan county who had had witnessed ventricular fibrillation arrest before emergency medical services were undertaken to investigate this 3-phase model with regard to bystander cardiopulmonary resuscitation (CPR). We hypothesized that the survival benefit from bystander CPR depends on the collapse-to-shock interval, with the highest benefit occurring during the circulatory phase. The collapse-to-shock interval was a priori grouped into 4 categories: 1 to 5, 6 to 7, 8 to 10, and ≥11 minutes. We used logistic regression analysis to assess whether the association between CPR and survival to hospital discharge depended on the collapse-to-shock interval category. Of the 2,193 events meeting the inclusion criteria, 67.0% had received bystander CPR. The average collapse-to-shock interval was 8.2 ± 2.8 minutes. The survival rate was 33.4%. A higher likelihood of survival was associated with bystander CPR (odds ratio [OR] 1.41, 95% confidence interval [CI] 1.15 to 1.73) and a shorter collapse-to-shock interval (OR −1.84, 95% CI 1.62 to 2.10, for each additional SD of 2.8 minutes less) after adjustment. The beneficial association of CPR increased as the collapse-to-shock interval increased (p = 0.05 for interaction). The bystander CPR was associated with an OR of survival of 0.96 (95% CI 0.64 to 1.46) for a 1- to 5-minute collapse-to shock interval, OR of 1.25 (95% CI 1.00 to 1.58) for a 6- to 7-minute interval, OR of 1.62 (95% CI 1.25 to 2.11) for an 8- to 10-minute interval, and OR of 2.11 (95% CI 1.32 to 3.37) for an ≥11-minute interval. The results of this investigation support a phased model of ventricular fibrillation arrest. The findings suggest that the transition from the electrical to circulatory phase may occur at about 5 minutes, and the circulatory phase may extend to 15 minutes. **(Am J Cardiol 2006;98:497–499)**

Accumulating evidence has suggested that the pathophysiology of ventricular fibrillation cardiac arrest may consist of 3 time-sensitive phases: electrical, circulatory, and metabolic.[1] The 3 phases form a continuum in which each phase describes the predominant dysfunction and in turn may indicate the most suitable therapy. According to this model, the electrical (first) phase is most effectively treated with rapid defibrillation. During the circulatory (second) phase, the outcome may improve by delaying defibrillation to perform cardiopulmonary resuscitation (CPR). Although the precise mechanism is uncertain, CPR during the circulatory phase may "prime" the heart for defibrillation by restoring some measure of oxygenated blood flow.[2] During the metabolic (third) phase, advanced brain and cardiac cell injury may attenuate the survival benefit of CPR. Thus, the benefit of CPR may occur predominantly during the circulatory phase, with little or no effect during the electrical or metabolic phases. We investigated this 3-phase model with regard to bystander CPR. Using this model, we hypothesized that the potential survival benefit of bystander CPR would depend on the interval from collapse to shock, with the greatest benefit occurring during the circulatory phase.

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This study was a retrospective, observational analysis of patients ≥18 years residing in a large metropolitan county who had had witnessed ventricular fibrillation cardiac arrest from January 1, 1990 to December 31, 2004. We were interested in accurately estimating the collapse-to-shock interval. We excluded unwitnessed ventricular fibrillation, because the collapse time would be unknown. Cardiac arrests that occurred after the arrival of the emergency medical services (EMSs) were excluded because we were evaluating the role of bystander CPR. The investigators' institutional review board approved the study. The EMS system is 2-tiered and follows the American Heart Association guidelines, which prioritize rhythm analysis and, if indicated, shock.[3]

The EMS maintains a surveillance system of EMS-treated cardiac arrests in which it reviews the dispatch tapes, first- and second-tier EMS reports, hospital discharge summaries, and death certificates.[4] Data are abstracted using the

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Table 1
Characteristics according to collapse-to-shock interval and bystander cardiopulmonary resuscitation (CPR) status

Characteristic	1–5 min		6–7 min		8–10 min		>11 min	
	No Bystander CPR (n = 70)	Bystander CPR (n = 103)	No Bystander CPR (n = 297)	Bystander CPR (n = 523)	No Bystander CPR (n = 258)	Bystander CPR (n = 595)	No Bystander CPR (n = 93)	Bystander CPR (n = 248)
Age (yrs)	63.9 ± 14.2	65.7 ± 13.1	63.9 ± 14.6	65.0 ± 13.7	66.5 ± 13.4	64.5 ± 13.5	68.6 ± 13.6	63.6 ± 13.6
Men (%)	77% (54)	78% (80)	78% (231)	79% (420)	83% (215)	78% (466)	83% (77)	79% (195)
Location* (%)								
Residence	30% (21)	34% (35)	69% (204)	45% (240)	84% (217)	64% (380)	77% (72)	64% (158)
Public	67% (47)	57% (59)	27% (80)	45% (238)	14% (37)	30% (177)	18% (21)	31% (76)
Facility	3% (2)	9% (9)	4% (13)	10% (51)	2% (4)	6% (38)	3% (3)	5% (14)
Collapse to shock†								
Interval 1	1.1 ± 0.3	1.1 ± 0.2	1.1 ± 0.5	1.2 ± 0.4	1.3 ± 0.6	1.3 ± 0.6	1.5 ± 1.1	1.9 ± 2.5
Interval 2	2.1 ± 0.9	2.3 ± 0.8	4.0 ± 0.8	4.1 ± 0.8	5.7 ± 1.0	5.7 ± 1.0	7.7 ± 2.1	8.4 ± 3.0
Interval 3	1.0 ± 0.5	1.1 ± 0.5	1.4 ± 0.5	1.4 ± 0.5	1.6 ± 0.6	1.7 ± 0.6	3.1 ± 3.6	2.7 ± 2.7
Cumulative interval	4.3 ± 0.7	4.5 ± 0.7	6.6 ± 0.6	6.6 ± 0.6	8.6 ± 0.7	8.7 ± 0.7	12.3 ± 2.8	13.0 ± 3.9
Collapse to CPR interval‡	3.7 ± 1.2	1.6 ± 1.0	5.4 ± 1.3	2.0 ± 1.3	7.2 ± 1.4	2.2 ± 1.5	8.4 ± 3.0	2.8 ± 2.9

Data are presented as means ± SDs or percentages (numbers of patients).
* Facility included medical clinic and nursing home.
† Interval 1 is collapse to 9-1-1 dispatch call receipt. Interval 2 is call receipt to EMS arrival on scene. Interval 3 is EMS on scene to shock.
‡ Although analysis and shock are priority, EMSs routinely begin CPR while defibrillator is being applied; hence, interval to CPR was typically less than interval to shock even in no bystander CPR group.

Utstein definitions.[5] Bystander CPR status is determined by the first-arriving EMS. The interval from collapse to call receipt is an estimate determined from the dispatch report. For most witnessed arrests, it was estimated as 1 minute. For cases in which the dispatch record revealed evidence of a delay between witnessing the collapse and calling 911, longer intervals were recorded. The interval from call receipt to scene arrival at curbside was provided by the electronic dispatch recording system and was verified on the EMS report. The interval from arrival on the scene until shock was abstracted from the EMS report. The cumulative collapse-to-shock interval was calculated by adding the 3 intervals. The interval times were estimated to the nearest minute.

We used descriptive statistics to evaluate the distribution of case characteristics according to bystander CPR and the collapse-to-shock interval. A sample of intervals was missing (215 for the collapse to call receipt and 921 for the scene arrival to shock). The values for missing intervals were generated using imputation.[6] Initially, the collapse-to-shock interval was modeled continuously. To help evaluate the relation among survival, bystander CPR, and collapse-to-shock interval, we a priori grouped the collapse-to-shock interval into 4 categories: 1 to 5, 6 to 7, 8 to 10, and ≥11 minutes. In a post hoc assessment, we subdivided the longest interval into 11 to 14 minutes and ≥15 minutes.

We used logistic regression analysis to assess whether the association between CPR and survival to hospital discharge depended on the collapse-to-shock interval category. In this model, we assessed whether the addition of an interaction term (bystander CPR × collapse-to-shock interval category) improved the fit of the model that included age, gender, location, bystander CPR, and collapse-to-shock interval category. Sensitivity analyses included only those events with complete information. Data were analyzed using STATA, version 8.0 (STATA Corp., College Station, Texas).

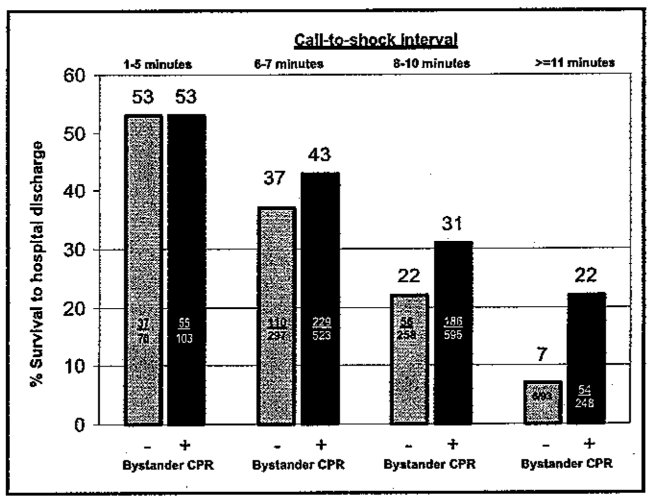

Figure 1. Survival to hospital discharge according to bystander CPR status and collapse-to-shock interval.

A total of 2,193 witnessed ventricular fibrillation arrests due to heart disease occurred before EMS arrival during the 15 years of the study. The average age was 64.9 ± 13.8 years, 1,738 of the 2,193 patients (79.3%) were men, 735 of 2,193 events (33.5%) occurred in a public location, 1,469 of 2,193 patients (67.0%) received bystander CPR, and the average collapse-to-shock interval was 8.2 ± 2.8 minutes. The survival to discharge rate was 33.4% (733 of 2,193). The characteristics according to CPR status and interval grouping are listed in Table 1. Overall, a higher likelihood of survival was associated with bystander CPR (odds ratio [OR] 1.41, 95% confidence interval [CI] 1.15 to 1.73) and shorter collapse-to-shock interval (OR 1.84, 95% CI 1.62 to 2.10 for 1 SD [2.8 minutes] less) after adjustment for age, gender, and location.

Figure 1 presents the survival to hospital discharge rate according to bystander CPR status and collapse-to-shock interval category. A single interaction between bystander CPR and collapse-to-shock interval significantly improved the fit of the model ($p = 0.05$), indicating that the beneficial association of CPR increased as the collapse-to-shock interval increased. Applying the interaction term to determine the OR of survival within each collapse-to-shock interval group, bystander CPR compared with no bystander CPR was associated with an OR of survival of 0.96 (95% CI 0.64 to 1.46) for the 1- to 5-minute collapse-to-shock interval, OR of 1.25 (95% CI 1.00 to 1.58) for the 6- to 7-minute interval, OR of 1.62 (95% CI 1.25 to 2.11) for the 8- to 10-minute interval, and OR of 2.11 (95% CI 1.32 to 3.37) for the ≥11-minute interval after adjustment for age, gender, and location. The results were similar when the analysis was restricted to those with complete data ($p = 0.02$ for interaction between collapse-to-shock interval group and bystander CPR).

We did not observe evidence of attenuation in the relative survival benefit of CPR for the longest prespecified collapse-to-shock interval category (Figure 1), as might be expected with the metabolic phase. Therefore, we stratified the ≥11 minute group to 11 to 14 and ≥15 minutes. In the 11- to 14-minute group, the survival rate was 26% (54 of 209) for the bystander CPR group and 7% (6 of 81) for the no bystander CPR group. No patients in either CPR group with a collapse-to-shock interval ≥15 minutes survived ($n = 51$).

Of the 733 hospital survivors, 647 (88%) had information about the location of discharge. Of the 647, 540 (83%) were discharged home instead of to a care facility. No difference was detected with regard to discharge location according to bystander CPR status within each collapse-to-shock interval category.

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In this observational study, we observed evidence supporting a phased model of ventricular fibrillation arrest. Specifically, the benefit of citizen CPR appeared to depend in part on the collapse-to-shock interval. Bystander CPR was not associated with a survival benefit during the first 5 minutes; rather, the relative benefit of bystander CPR increased steadily as the collapse-to-shock interval increased.

The results of this study have confirmed the importance of early defibrillation and bystander CPR because the 2 were significantly and substantially associated with survival.[7] Moreover, the results have suggested that the relative benefit of bystander CPR increases as the patient transitions from the electrical to the circulatory phase and then progresses through the circulatory phase. We were not able to, a priori, detect a later (metabolic) phase in which the bystander CPR benefit was attenuated. One explanation is that CPR started soon after collapse (as is the case for most bystander CPR in witnessed arrests) substantially offsets the metabolic phase. To this extent, no patients in the group with a collapse-to-shock interval of ≥15 minutes survived, regardless of bystander CPR status.

This study had limitations. The investigation was retrospective and observational, hence unaccounted for confounding factors may have influenced the findings. To address this, we adjusted for potential confounders (age, gender, location) and restricted the analysis to witnessed arrests. Some intervals were estimated or imputed. These intervals accounted for a modest portion of the total collapse-to-shock intervals and had a fairly small distribution. Moreover, any misclassification of intervals would likely attenuate the interaction observed in this investigation. Citizen bystanders provided CPR, and the quality could not be confirmed. The quality of bystander CPR may influence survival.[7] We had limited data on the neurologic outcomes of survivors, although the location of discharge (home vs other), a rough surrogate, did not differ by bystander CPR status within the collapse-to-shock interval categories. Finally, the EMS system is relatively mature, and caution should be used when generalizing these findings.

The results of this investigation support a phased model of ventricular fibrillation arrest and suggest that the transition from the electrical to circulatory phase may occur at about 5 minutes and the circulatory phase may extend to 15 minutes. These findings underscore the evolving paradigm that optimal resuscitation may be achieved when therapy is tailored to the physiologic phase of the arrest. The formidable challenges are how to readily identify the predominant pathophysiology of a specific patient and, in turn, provide the best care.

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