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Survival from prehospital cardiac arrest is critically dependent upon response time☆

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KEYWORDS
Prehospital cardiac arrest;
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Summary
Study objective: This study correlated the delay in initiation of bystander cardiopulmonary resuscitation (ByCPR), basic (BLS) or advanced cardiac (ACLS) life support, and transport time (TT) to survival from prehospital cardiac arrest. This was a secondary endpoint in a study primarily evaluating the effect of bicarbonate on survival.
Design: Prospective multicenter trial.
Setting: Patients treated by urban, suburban, and rural emergency medical services (EMS) services.
Patients: Eight hundred and seventy-four prehospital cardiac arrest patients.
Interventions: This group underwent conventional ACLS intervention followed by empiric early administration of sodium bicarbonate noting resuscitation times. Survival was measured as the presence of vital signs on emergency department (ED) arrival. Data analysis utilized Student's t-test and logistic regression ($p < 0.05$).
Results: Survival was improved with decreased time to BLS (5.52 min versus 6.81 min, $p = 0.047$) and ACLS (7.29 min versus 9.49 min, $p = 0.002$) intervention, as well as difference in time to return of spontaneous circulation (ROSC). The upper limit time interval after which no patient survived was 30 min for ACLS time, and 90 min for transport time. There was no overall difference in survival except at longer arrest times when considering the primary study intervention bicarbonate administration.
Conclusion: Delay to the initiation of BLS and ACLS intervention influenced outcome from prehospital cardiac arrest negatively. There were no survivors after prolonged delay in initiation of ACLS of 30 min or greater or total resuscitation and transport time of 90 min. This result was not influenced by giving bicarbonate, the primary study intervention, except at longer arrest times.

☆ A Spanish translated version of the summary of this article appears as Appendix in the online version at 10.1016/j.resuscitation.2005.08.014.

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Introduction

The use of prehospital health care providers to intervene in acute cardiac emergencies has historically been a focus of emergency care. Eisenberg et al. reported the results of an evaluation of prehospital care by emergency medical technicians (EMT) compared to that delivered after the addition of paramedic skills, such as defibrillation, tracheal intubation and drug administration.[1] They reported an improved rate of survival to the coronary care unit (CCU) (19—34%) and rate of hospital discharge (7—17%), which they related to a decrease in delay to advanced care delivery which was decreased to one-third from 27.5 to 7.7 min.

However, Dean et al. reported on the outcome of 134 patients who received mobile paramedic unit care compared to control patients without paramedic intervention demonstrating no change in outcome by multiple logistic regression analysis.[2] Defibrillation was the only beneficial intervention identified, but also added a 29 min delay to hospital arrival suggesting the need for more streamlined care.

Later, Shuster and Chong went on to evaluate 15 prehospital studies over the early years of emergency medical care suggesting no benefit of prehospital administration of any of a number of common prehospital medications.[3] Qualitatively, there have been few studies that have examined the use of such agents as albuterol, bicarbonate, bronchodilator agents, diazepam, dobutamine, dopamine, glucose, isoproterenol, naloxone, or nitrous oxide for their prehospital efficacy.[4]

There are four factors that are related to the ability to resuscitate patients in the prehospital arrest setting. They include decreasing the time to starting rescue procedures, use of electrical defibrillation, accuracy of technique of basic life support (BLS), and ventilation efficacy.[5]

The ''early defibrillation'' controversy has once again raised interest in use of first responders or EMT in a two-tier response system. Wilson et al. evaluated 126 patients whose care was limited to BLS: mask oxygen, IV fluids, external chest compressions, and artificial respiration.[6] The survival rate was 22% (28) to hospital admission and 9% (11) to hospital discharge, with a favorable prognosis identified to include an initial rhythm of ventricular fibrillation or tachycardia, 14% (7 of 50); initial blood pressure >90 mmHg and pulse rate >50 bpm, 50% (3 of 6). However, if the patient was in cardiac arrest then cardiopulmonary resuscitation (CPR) did not change outcome.

Thus, the issue becomes a question of whether resuscitation endpoint can be determined past which no patient survives.

Methods

This prospective, randomized multicenter clinical trial involved cardiac arrest patients encountered by EMT-Ps in a prehospital setting, and transported to hospitals within the study area, usually within a 5—30 min radius. Patients were randomized individually to a treatment group receiving an empiric dose of bicarbonate (Abbott, USA) 1 ample (50 mEq/L) early in the arrest cycle (Figure 1).

The demographics treatment and clinical variables related to outcome were analyzed including, response to bicarbonate administration, scene factors, response time, cardiopulmonary variables, procedures, and duration of arrest. Patient outcome was recorded as the return of spontaneous circulation measured as palpable pulses and initial emergency department survival (discharge), as a primary endpoint.

Specifically, resuscitation intervention times were recorded as a secondary endpoint by the paramedic as estimated time of arrest (arrest time, AT), time until institution of bystander CPR (ByCPR), basic life support, advanced cardiac life support (ACLS), return of spontaneous circulation (ROSC) and scene to hospital transport time (TT) measured from arrest to hospital arrival time. In addition, ACLS intervention time is subcategorized into short-term (0—5 min), moderate (5—15 min), and long-term (>15 min) response for further analysis.

Examining these same issues according to the Office for Protection from Research Risk (OPRR) Guidelines suggest further qualification to waive prospective informed consent according to the second wavier condition of 45 CFR 46.116 section D.[8] (1) The research involves no more than minimal risk to the subjects. (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects. (3) The research practicably could not be carried out without the waiver or alteration. (4) Whenever appropriate, the subjects are provided with additional information after participation.

Numerical data were represented as means and standard deviation with Student's *t*-test, Fisher's exact, Chi square with Pearson correlation tests used for logistic regression intergroup comparison (alpha < 0.05) (SPSS/PC+®, Chicago, IL). The study results were examined by the investigators at 3-month intervals (or 25% of projected patients) to

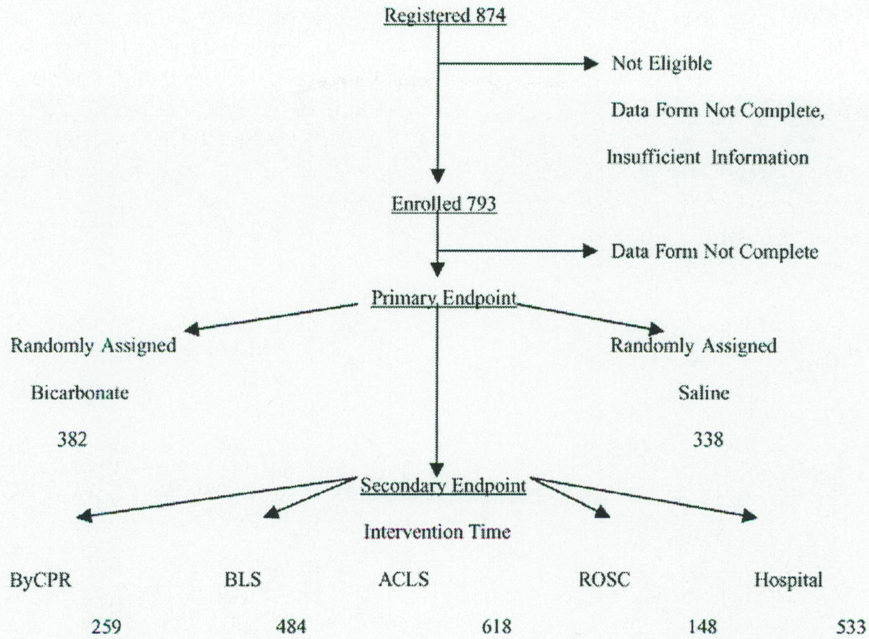

Figure 1 Trial profile.

verify early trends and outcome with capability of later modification.

Results

There were no significant differences in baseline pre-experimental demographic or cardiopulmonary variables in groups who were randomized to receive bicarbonate or not.

Overall, 874 patients were enrolled with an average age of 67.6 ± 15 (3–101) years and weight of 89.6 ± 40.3 kg. The response time to cardiopulmonary intervention did not correlate to bicarbonate administration as expected with randomization. The cumulative survival rate was 13.9% (110 of 792) with 82 (9.4%) patients excluded for lack of complete information on documentation.

The mean time to resuscitative intervention was 2.08 ± 2.77 (0–21) min for ByCPR, 6.62 ± 5.73 (0–35) min for BLS, 9.08 ± 6.31 (0–40) min for ACLS, 24.96 ± 13.55 (0–98) min for ROSC, and 41.05 ± 11.68 (0–92) min for hospital transport time (Table 1). Survival improved with decreased time to BLS intervention (5.52 min versus 6.81 min, $p = 0.047$) and ACLS intervention (7.29 min versus

Table 1 Response time correlation to ER survival

	Time interval				*t*-Test (*p*)
	Mean (min)	Range (min)	Survivors (min)	Non-survivors (min)	
ByCPR *N* = 259	2.08 ± 2.77	0–21	1.58 ± 1.71 39	2.20 ± 2.79 189	0.07
BLS *N* = 484	6.63 ± 5.73	0–35	5.52 ± 4.75 570	6.81 ± 5.66 361	0.047
ACLS *N* = 618	9.08 ± 6.31	0–40	7.29 ± 5.76 88	9.49 ± 6.30 475	0.002
ROSC *N* = 148	4.96 ± 13.55	0–98	27.27 ± 13.71 77	20.73 ± 12.82 56	0.006
Hospital *N* = 533	41.05 ± 11.68	0–92	39.69 ± 12.91 78	41.65 ± 11.31 402	0.214

Table 2 ACLS resuscitation interval correlated to ER survival

ACLS time (min)	Non-survival	Survival	
0–8	227 (80.2)	56 (19.8)	283 (50.3)
<8	248 (88.6)	32 (11.4)	280 (49.7)
	475 (84.4)	88 (15.6)	563 (100)

Values in parenthesis are in percentages. Chi square Pearson correction. $p = 0.0063$; $p =$ NS bystander CPR (<2 min), BLS (<4 min).

9.49 min, $p = 0.002$), while the time to ByCPR only approached significance (1.58 min versus 2.20 min, $p = 0.07$) (Table 1).

For those patients who respond to intervention and survive, the time until ROSC was increased compared to those who have ROSC and then do not survive (27.27 min versus 20.73 min, $p = 0.0006$). The time interval after which no patient was able to survive was 25 min for ACLS and 40 min for transport time.

A convenience grouping of resuscitation interval data suggest that previously established benchmarks for ByCPR (<2 min, $p = 0.375$) and BLS (<4 min, $p = 0.006$) are not associated with improved survival, while provision of ACLS (<8 min, $p = 0.006$) is strongly correlated with improved survival (Table 2).[7]

In fact, experimental classification of ACLS resuscitation interval finds a significant reduction in survival comparing short (24.0%) to moderate (12.7%) duration arrest with a 47% decrease in relative risk of mortality, while a less significant reduction was noted compared to long-term arrest (9.1%) with a 28% decrease in relative risk (Table 3). There was no overall difference in survival with bicarbonate administration unless there was prolonged (>15 min) resuscitation time.

Table 3 Time to ACLS correlated to ER survival

ET ACLS	ER survival		
	Non-survival	Survival	
Short-term (0–5 min)	130 (76.0)	41 (24.0)	171 (30.4)
Moderate (5–15 min)	275 (87.3)	40 (12.7)	315 (56.0)
Long-term (>15 min)	70 (90.9)	7 (9.1)	77 (13.7)
	475 (84.4)	88 (15.6)	563 (100.0)

Values in parenthesis are in percentages. Chi square Pearson correction. $p = 0.00112$.

Discussion

Clearly, there is a wide discrepancy in the rates of survival in in-hospital compared to prehospital cardiac arrest events. Rosenberg et al. evaluated 300 hospitalized patients demonstrating a 54% initial post-CPR survival followed by 23% survival to hospital discharge.[9] Predictors of good resuscitation outcome include initial ventricular tachycardia or fibrillation, and brief duration of cardiac arrest CPR < 30 min.

Wright found response times of less than 4 min resulted in improved survival to discharge in 23.1 compared to 7.0% of VF/VT events, and 30.8 compared to 7.7% of other arrhythmic events.[10] Likewise, the use of ByCPR improved outcome from 23.1 to 42.9% in VF/VT and 7.7 to 15.8% when ACLS providers arrived within 4 min.[10]

Similar survey data from the study by Valenzuela et al. of 372 prehospital patients demonstrated a 20% survival rate to hospital admission and 6% survival to discharge.[11] This rate improved to 26% for hospital admission and 10% for hospital discharge in witnessed events, and 38 and 15%, respectively, for witnessed ventricular fibrillation.

Van der Hoeven et al. conducted a retrospective chart review of 309 adult patients where the 13.6% survived to hospital discharge was associated with a favorable prognosis with the arrest being witnessed, short call response interval, initial cardiac rhythm of VF or VT, and the provision of appropriate ACLS care.[12] Improvement of all aspects of the ''prehospital chain of survival'' is likely to result in better outcome.

Perhaps the most important consideration in outcome prediction in adult prehospital cardiac arrest is the time until definitive resuscitation intervention is begun. One such measure is scene time (ST) evaluated by Spaite et al. in 298 patients.[13] Here, only a minority (27.0%) of patients had ST < 12 min, but they were more likely to have ROSC (26.6% versus 15.9%) and were more likely to survive (13.9% versus 6.5%) compared to those on scene for more prolonged periods.

However, demographic analysis of prehospital arrests found deficiencies in documentation with reports filed on 89% with VF as the first recorded rhythm in 52% progressing to asystole or EMD in 86% yielding a 2% survival to hospital discharge.[5] They reported a median time to BLS of 6 min, call to response time of 8 min, call to ALS time of 2 min, and ST of 15 min for EMT and 31 min for EMT-P.

Likewise, survival to hospital discharge has been clearly related to the interval until therapeutic intervention. The periods from collapse until initiation of BLS (3.6 min versus 6.1 min) and until delivery of first defibrillation (4.3 min versus 7.3 min) were shorter in survivors, as well as noting improved projected survival from an early defibrillation linear regression model (3—28%).[14]

Clearly, one of the most dominant factors predicting outcome from cardiopulmonary arrest is the delay until resuscitation intervention. To elucidate the contribution of the interval to resuscitation and arrest outcome it was helpful to review other contributing factors. There were no other apparent differences in the pre-experimental treatment groups in regard to demographic factors in our study. This perhaps suggests a stronger, but not necessarily causal relationship between interval and outcome.

The overall survival rate of 13.9% (110 of 793) compares favorably to a 4.2 (1.7—13%) pooled analysis of 3220 prehospital patients suggesting improved prehospital outcome.[15] Benchmark times for resuscitative intervention suggest a 2 min response for ByCPR, 6 min BLS, 9 min ACLS, 25 min ROSC, and 40 min hospital transport as feasible targets for prehospital response as suggested by the author.

There appeared to be a positive association between a reduction in time to intervention specifically for BLS and ACLS care. The association ($p = 0.047$) with BLS providing airway assistance, oxygen and bag-valve mask ventilation, but excluding defibrillation, was defined and perhaps most related to the notification of more aggressive resuscitative care.[14]

On the other hand, the strongest association ($p = 0.004$) was between the provision of advanced cardiac care featuring defibrillation, intubation, intravenous access, and cardioactive medication administration. This care is provided by EMT-Ps rather than EMTs, fire personnel or other first responders.

Our study was not designed to elucidate which of these individual resuscitative interventions was most responsible for the increase in survival noted. However, the correlation to successful intubation was self-evident, as was the lack of correlation to intravenous access or other procedures, such as cardiac pacing.

Interestingly, this was perhaps a paradoxical response, whereby survivors had a longer delay until ROSC than non-survivors from 27 min versus 20 min post-initiation of resuscitation. Perhaps, the effect may suggest a factor other than early defibrillation that may be implicated in arrest survival. Therefore, in the arrest group who fail to respond to convention defibrillation, there may be additional time required to create an effective resuscitation milieu.

This delay allows time for adequate compressions to restore perfusion, accompanied by vasopressor use for acid—base correction.[16] This concept has been embodied by the intubation—compression before defibrillation scenario for resuscitation. The conclusion that individuals are more likely to be resuscitated after brief delay seems self-evident. However, the greatest value of these data are directed toward establishing specific discriminators for non-survival so that we may improve the direction of our resuscitative efforts.

There is a significant improvement in survival noted as time to resuscitation is decreased, increasing survival two-fold in Pell's Scottish trial and three-fold in Blackwell's mid-Atlantic EMS study.[17,18] Although convenience grouping data—ByCPR (<2 min), BLS (<4 min), ACLS (<8 min), and hospital transport (<40 min) are helpful as quality assurance markers they do not allow prediction of individual patient outcome. However, it is helpful to note that there appears to be a plateau effect where there is less than one-third variability in survival between moderate (5—15 min) and prolonged (>15 min) arrest.[19]

The best estimate of the upper limit or survival in the prehospital setting is that there are no survivors of normothermic arrest beyond an ACLS time interval of 30 min and transport time of 90 min.

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References

1. Eisenberg MS, Bergner L, Hallstrom A. Out of hospital cardiac arrest: improved survival with paramedic services. Lancet 1980:812—5.
2. Dean NC, Haug PJ, Hawker PJ. Effect of mobile paramedic units on outcome in patients with myocardial infarction. Ann Emerg Med 1988;17:61—8.
3. Shuster M, Chong J. Pharmacological intervention in prehospital care, a critical appraisal. Ann Emerg Med 1989;18:126—30.
4. Atkins JM. Emergency medical services systems in acute cardiac are state of the art. Circulation 1986;74:4—8.
5. Hodgetts TJ, Brown T, Driscoll P, Hanson J. Pre-hospital cardiac arrest: room for improvement. Resuscitation 1995;29:47—54.

6. Wilson BH, Severance HW, Raney MP, et al. Out of hospital management of cardiac arrest by basic emergency medical technicians. Am J Cardiol 1984;53:68—70.
7. Roth R, Stewart RD, Rogers K, et al. Out of hospital cardiac arrest: factors associated with survival. Ann Emerg Med 1984;13:237—43.
8. Office for Protection from Research Risk (OPRR) Guidelines Federal Register 45 CFR 46.116 second.
9. Rosenberg M, Wang C, Hoffman-Wilde S, Hickham D. Results of cardiopulmonary resuscitation. Arch Intern Med 1993;153:1370—5.
10. Wright D, Bannister J, Ryder M, Mackintosh AF. Resuscitation of patients with cardiac arrest by ambulance staff with extended training in West Yorkshire. Br Med J 1990;301:600—2.
11. Valenzuela TD, Spaite DW, Meislin HW, Clark LL, Wright AL, Ewy GA. Case and survival definitions in out of hospital cardiac arrest. J Am Med Assoc 1992;267:272—4.
12. van der Hoeven JG, Waanders H, Compier EA, van der Weyden PK, Meinders AE. Evaluation of an emergency medical system. The prognosis in patients with an out of hospital cardiac arrest. Netherlands J Med 1994;44:5—11.
13. Spaite DW, Criss EA, Valenzuela TD, Meislin HW, Ross J. Analysis of prehospital scene time and survival from out of hospital, non-traumatic, cardiac arrests. Prehosp Disast Med 1991;6:21—8.
14. Weaver WD, Cobb LA, Hallstrom AP, Fahrenbruch C, Copass MK, Ray R. Factors influencing survival after out of hospital cardiac arrest. J Am Col Cardiol 1986;7:752—7.
15. Vukmir RB. Survival and outcome from prehospital cardiac arrest. Emerg Med J 2004;21:370—3.
16. Vukmir RB, Bircher N, Safer P. Sodium bicarbonate in cardiac arrest: a reappraisal. Am J Emerg Med 1996;14:192—206.
17. Pell JP. Effect of reducing ambulance response time on deaths from out of hospital cardiac arrest: cohort study. Br Med J 2001;322:1385.
18. Blackwell TH. Response time effectiveness: comparison of response time and survival in an urban emergency medical services system. Acad Emerg Med 2002;9:288.
19. Vukmir RB, Bircher N, Radovsky A, Safar P. Sodium bicarbonate may improve outcome in dogs with brief or prolonged cardiac arrest. Crit Care Med 1995;23:515—22.