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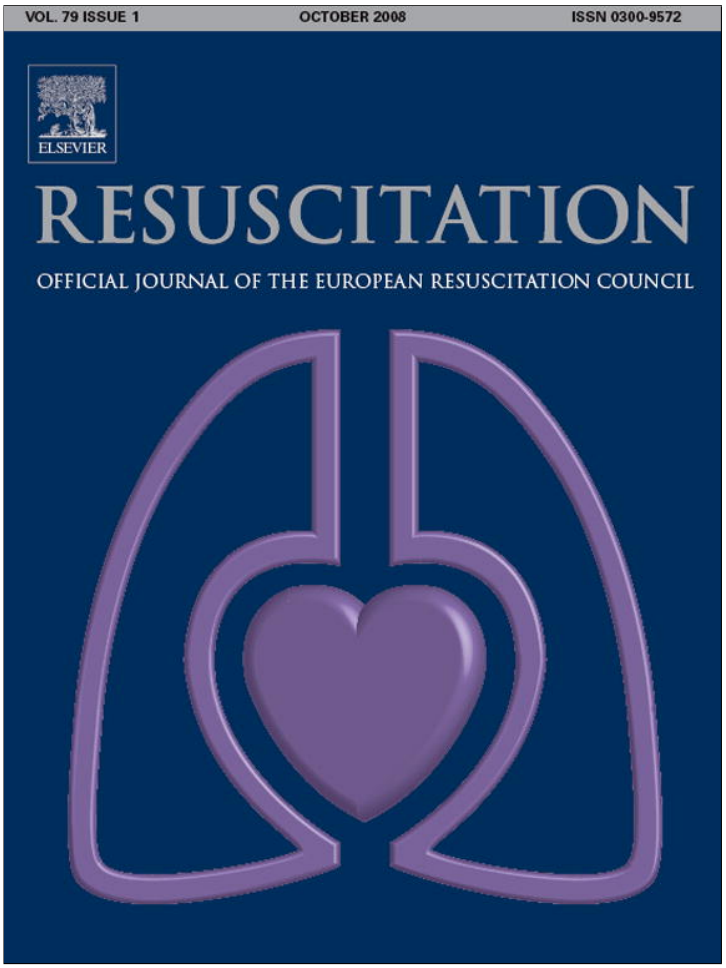

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CLINICAL PAPER

The impact of prehospital transport interval on survival in out-of-hospital cardiac arrest: Implications for regionalization of post-resuscitation care☆,☆☆

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Summary
Objective: There is growing evidence that therapeutic hypothermia and other post-resuscitation care improves outcomes in out-of-hospital cardiac arrest (OHCA). Thus, transporting patients with return of spontaneous circulation (ROSC) to specialized facilities may increase survival rates. However, it is unknown whether prolonging transport to reach a designated facility would be detrimental.
Methods: Data from OHCA patients treated in EMS systems that cover approximately 70% of Arizona's population were evaluated (October 2004—December 2006). We analyzed the association between transport interval (depart scene to ED arrival) and survival to hospital discharge in adult, non-traumatic OHCA patients and in the subgroup who achieved ROSC and remained comatose.
Results: 1846 OHCA occurred prior to EMS arrival. Complete transport interval data were available for 1177 (63.8%) patients (study group). 253 patients (21.5%) achieved ROSC and remained comatose making them theoretically eligible for transport to specialized care. Overall, 70 patients (5.9%) survived and 43 (17.0%) comatose ROSC patients survived. Mean

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transport interval for the study group was 6.9 min (95% CI: 6.7, 7.1). Logistic regression revealed factors that were independently associated with survival: witnessed arrest, bystander CPR, method of CPR, initial rhythm of ventricular fibrillation, and shorter EMS response time interval. There was no significant association between transport interval and outcome in either the overall study group (OR = 1.2; 0.77, 1.8) or in the comatose, ROSC subgroup (OR 0.94; 0.51, 1.8).
Conclusion: Survival was not significantly impacted by transport interval. This suggests that a modest increase in transport interval from bypassing the closest hospital en route to specialized care is safe and warrants further investigation.
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Introduction

For many years it was thought that the only significant determinants of survival from out-of-hospital cardiac arrest (OHCA) occurred in the prehospital setting.[1,2] Even with the restoration of spontaneous circulation a sense of futility often prevents aggressive in-hospital post-resuscitation care in patients without an immediate return of cerebral activity.[3–6] Recent evidence, however, suggests that survival and neurological outcome can be dramatically improved by in-hospital post-resuscitation care despite persistent coma after arrest.[7–9] Subsequently, consideration has been given to bypassing local hospitals en route to regional cardiac arrest centers staffed and equipped to provide specialized post-resuscitation care.[10,11] The question remains whether it is detrimental to prolong the transport of critically ill ROSC patients.

Numerous EMS leaders in Arizona have suggested developing regional ''Cardiac Arrest Centers'' and EMS protocols aimed at taking comatose ROSC patients to these centers for specialized post-resuscitation care. However, we have been able to find only one evaluation of the association between TI and outcome in OHCA within the peer-reviewed literature.[10] This prompted us to analyze our statewide OHCA database with the intent of identifying evidence for the safety of increased time spent in transport.

Methods

The State of Arizona, through its Bureau of Emergency Medical Services and Trauma System, initiated a statewide, prospective observational cohort study of OHCA victims on whom resuscitation was attempted in the field. The Save Hearts in Arizona Registry & Education (SHARE) Program database contains information on OHCA patients from 48 EMS agencies/fire departments responsible for responding to prehospital medical emergencies for approximately 70% of the 5.5 million residents of the state.

A standardized data collection tool was prospectively developed and study variables were defined for OHCA. Entry criteria, time intervals, and nodal events conform to the Utstein Style.[12] Participating EMS agencies sent the first care form for each OHCA to the SHARE Program Research and Quality Improvement Director. Data were manually abstracted by the director from the EMS first care forms and entered into a Microsoft Access™ (Microsoft, Inc., Redmond, WA) database. Cases were excluded if resuscitation was not initiated, the patient had a Do-Not-Resuscitate order, the etiology of the arrest was known to be non-cardiac, or the arrest was witnessed by EMS providers. Outcome data were obtained from the Arizona Department of Health Services (ADHS) Office of Vital Statistics. When no death confirmation occurred after 3 months, survival was verified by patients' medical records from the receiving hospital. Verification of survival or death due to insufficient documentation occurred in less than 2% of the cases. The detailed methodology of data collection for the SHARE database has been published elsewhere.[13] The database has been used to evaluate multiple changes in OHCA care in the state.[14–17] While not directly related to this analysis, it is worth noting that part of the purpose of the registry was to evaluate the impact of a novel EMS protocol (cardiocerebral resuscitation) on outcome. Cardiocerebral resuscitation for EMS providers includes 200 pre-shock chest compressions, a single shock followed immediately by 200 post-shock chest compressions, delayed endotracheal intubation and early intravenous epinephrine (adrenaline). The database contains patients receiving standard CPR/ACLS care and others receiving cardiocerebral resuscitation.[13,14,16,17]

Pertinent variables were analyzed for patients presenting from October 2004 through December 2006. Additional exclusions for this analysis were patients less than 18 years of age or if there were data missing that were required for the analysis. TI (EMS unit leaves scene until arrival at the receiving hospital)[18] was analyzed to identify any potential association with patient outcomes. The analysis was also performed on patients who achieved ROSC, but remained comatose in the field, since this subgroup would theoretically bypass the closest hospital to be taken to a specialized post-resuscitation center.

Statistical analysis utilized SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL). Continuous variables are presented as mean ± standard deviation (S.D.) for those variables that are normally distributed. Variables that are not normally distributed are presented as medians with inter-quartile ranges. Multiple logistic regression analysis was performed to determine whether there was any causal association between TI and survival, adjusting for potential confounders. Factors that are potentially associated with survival were included in the logistic regression model. These included age, gender, witnessed arrest, bystander CPR, initial rhythm of ventricular fibrillation, the presence of shock, location of cardiac arrest, IV drugs received, the resuscitation protocol followed by EMS (standard BLS/ACLS versus cardiocerebral resuscitation), and EMS response interval. The final regression model included only variables significantly associated with survival (witnessed arrest,

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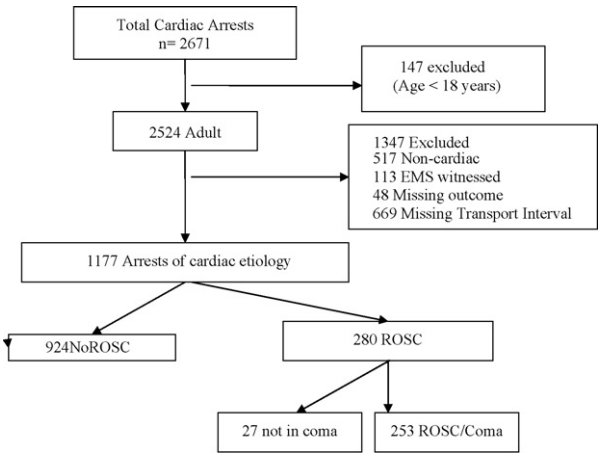

Figure 1 Out-of-hospital cardiac arrest database.

bystander CPR, initial rhythm of ventricular fibrillation, the method of EMS resuscitation, and EMS response interval).

The *a priori* alpha level considered statistically significant was 0.05. The study, methods of data collection, and publication of the data were approved by the ADHS Human Subjects Research Board and the University of Arizona Investigational Review Board.

Results

Figure 1 shows the cases that were entered into the database during the study period. 1846 were adults with OHCA of presumed cardiac etiology occurring prior to EMS arrival. Among these cases, 1177 (63.8%) had complete TI data and this cohort comprised the overall study group. Table 1 shows the demographics, event characteristics, initial cardiac rhythms, and patient outcomes. 280 patients achieved ROSC (23.8%). 253 patients (21.5%) achieved ROSC but remained comatose and would have been potential candidates for transport to a specialized cardiac arrest center. Overall, 70 patients (5.9%) survived to hospital discharge and 43 (17.0%) comatose ROSC patients survived to hospital discharge.

The demographics and event characteristics for the study group and the subgroup of comatose ROSC patients is shown in Table 1. The time interval data are shown in Table 2. The mean response interval was 5.4 min and the mean TI was 6.9 min.

Logistic regression identified the variables that were independently associated with the probability of survival. These included witnessed arrest: odds ratio (OR): 5.9; 95% confidence intervals: 2.8, 12.3; the presence of bystander CPR: 2.2 (1.3, 3.7); initial rhythm of ventricular fibrillation: 3.0 (1.7, 5.2); intravenous drugs received: 3.3 (1.1, 9.5); cardiocerebral resuscitation by EMS: 2.6 (1.5, 4.4); and response interval: 0.43 (0.25, 0.73).

In the study cohort as a whole, adjusting for the covariates that were independently associated with survival using step-wise logistic regression, no causal relationship was identified between TI and survival (OR = 1.2; 0.77, 1.8). In addition, logistic regression revealed no causal association between TI and survival in the subgroup of comatose ROSC patients (OR = 0.94; 0.51, 1.8).

Discussion

For decades, despite remarkable survival rates in a few settings,[19,20] the vast majority of systems have reported dismal survival rates for OHCA.[21–25] Additionally, many experts have considered prehospital care to be the only significant determinant of survival. In 1988, Kellerman and associates identified that OHCA patients who failed to be successfully resuscitated in the field had essentially no chance of being resuscitated in the hospital. This led to the conclusion that, ''Virtually all of the progress made to date in the management of out-of-hospital cardiac arrest has come from

Table 1 Demographic and event characteristics

Demographics and event characteristics	All OHCA patients $n = 1177$ Mean (95% CI) or % (#)	OHCA ROSC comatose patients ($n = 253$)
Mean age (years)	66.1 (65.2—67.0)	67.1 (65.4—68.7)
Male sex, % (*n*)	66.9 (788)	66.8 (169)
Witnessed, % (*n*)	50(588)	62.5 (158)
Bystander CPR, % (*n*)	38.7 (455)	42.3 (107)
Location (home), % (*n*)	71.2 (838)	68.4 (173)
Initial rhythm, % (*n*)		
VF	34.8 (410)	45.8 (116)
PEA	23.6 (2780	24.1 (61)
Asystole	41.0 (482)	29.2 (74)
Other	0.6 (7)	0.8 (2)
Outcome, % (*n*)		
Dead on scene	0.3 (3)	0
Died in ED	80.3 (945)	37.2 (94)
Died in hospital	13.5 (159)	45.8 (116)
Survived to discharge	5.9 (70)	17.0 (43)

OHCA = out-of-hospital cardiac arrest; VF = ventricular fibrillation; PEA = pulseless electrical activity; ED = emergency department.

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Table 2 EMS time intervals[a]

EMS time intervals (min)	All OHCA patients ($n = 1177$)		OHCA ROSC comatose patients ($n = 253$)	
	Mean (95% CI)	Median (25th–75th quartile)	Mean (95% CI)	Median (25th–75th quartile)
Response interval	5.4 (5.2–5.5)	5 (4–6)	4.9 (4.6–5.2)	5 (3–6)
On-scene Interval	18.3 (17.9–18.6)	18 (14–22)	19.1 (18.3–19.8)	18 (15–22)
Transport interval	6.9 (6.6–7.1)	6 (4–9)	6.9 (6.3–7.5)	6 (4–8)
Total prehospital interval	30.6 (30.1–31.1)	29 (25–34)	30.9 (29.8–32.0)	29 (25–35)

Response interval = call received to arrival on scene; on-scene interval = arrival on scene to leave scene; transport interval = leave scene to arrival at ED; total prehospital interval = call received at the public safety answering point (PSAP) to arrival at ED.
[a] Refs. [12] and [18].

developments in prehospital emergency cardiac care''.[1] This may be a major reason why, even with ROSC, in the absence of immediate clinical evidence of return of cerebral activity many patients do not receive aggressive post-resuscitation care. This fact has been well established in patients who suffer cardiac arrest in the hospital setting.[4,6] Peberdy and Ornato discovered that: ''An astonishing percent of patients, who initially survive an in-hospital cardiac arrest are made ''Do Not Attempt Resuscitation'' (DNAR), often so early after ROSC that there is inadequate time to determine whether the patient will experience neurological recovery''.[3] They went on to describe data from the National Registry of Cardiopulmonary Resuscitation (NRCPR) revealing that, ''63% of patients who survive a cardiac arrest in the hospital are given a DNAR status and 43% have care actively withdrawn, often in patients who are young, have no terminal illness and had an otherwise well executed, successful resuscitation.... The majority of patients who achieve ROSC are being abandoned long before it is even reasonable to attempt to predict neurological recovery''.[3]

Years of EMS research have shown the profound impact of several prehospital interventions.[14,20,24] There is now growing evidence that, if circulation can be successfully restored in the field, survival from OHCA can also be dramatically impacted by in-hospital post-resuscitation care.

Two randomized controlled trials (RCTs) have demonstrated marked improvement in survival and neurologic outcome when victims of witnessed prehospital ventricular fibrillation receive therapeutic hypothermia (TH).[26,27] Subsequent meta-analyses, systematic reviews, and quasi-experimental investigations have lent further support to the dramatic improvement in outcome from this relatively simple procedure in patients with ROSC who remain comatose after cardiac arrest.[28–31] In response, several consensus processes have supported the use of mild TH.[6,32] Despite the clear evidence from two randomized, controlled trials and the endorsement of the American Heart Association and the International Liaison Committee on Resuscitation (ILCOR), TH is used in only a small minority of patients who are comatose after cardiac arrest.[31,33]

There is also growing evidence that other post-resuscitation interventions may significantly improve outcome, especially when the management of ROSC patients is standardized. These include optimization of body temperature, hemodynamics, blood glucose, acid–base status, and electrolytes along with anticonvulsant therapy, antiarrhythmic therapy, timely thrombolysis, percutaneous coronary interventions, coronary artery bypass grafting and intraaortic balloon counterpulsation.[7–9,34–39]

Sunde and associates reported marked improvement when prehospital ROSC patients subsequently received specialized post-resuscitation care. In their study, favorable neurological survival occurred in 56% of patients during the intervention period compared to only 26% during the control period.[37] The odds ratio for good outcome was 3.6 for those receiving specialized post-resuscitation care. Lurie and associates initiated a comprehensive cardiac arrest ''Resuscitation Center'' with an intentional, standardized approach to post-resuscitation care in a rural city in Minnesota. In the 12 months following inception of the program, 63% of 26 patients with witnessed ventricular fibrillation were discharged in good neurologic condition. This represented a 131% relative increase in survival among ROSC patients who arrived at the hospital in coma.[40]

While these systems have achieved impressive results, nearly all of the systems that have reported OHCA data have shown that the vast majority of patients who obtain ROSC in the field subsequently go on to die in the hospital.[20,24,26,27] This is also true of the EMS systems in Arizona where 83% of ROSC patients died after ED arrival. Thus, post-resuscitation care has enormous potential for impact since so many patients who achieve ROSC currently go on to die.

The growing evidence in support of specialized, coordinated post-resuscitation care has spawned discussions regarding the potential for regionalization like that which has occurred in trauma systems.[11] These discussions envision bypassing the ''local'' hospital en route to specialized regional cardiac arrest centers. An important consideration has been the potential downside of prolonging the transport of these critically ill patients. The history of EMS is replete with ''good ideas'' being implemented without solid confirmatory evidence, only to later uncover the fact that the ideas were of no benefit or were even harmful (e.g. Military Anti-Shock Trousers for trauma patients in shock).[41]

We have been able to identify only one study that directly evaluated the potential impact of TI on outcome in OHCA. While this was not the primary objective of the investigation, Davis and associates assessed this issue in 639 OHCA patients in San Diego, CA.[10] They found no difference in mean TI among ROSC patients who died in the ED (8.3 min), died after inpatient admission to the hospital (7.8 min), or survived to discharge (8.5 min). In addition, receiver-operator curve analysis identified no predictive ability of TI for hospital admission. Thus, they found no

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causal association between TI and patient outcomes. One of the differences in our analysis is that, while Davis evaluated all ROSC patients, we specifically identified those who remained comatose after ROSC and, therefore, would be considered for TH.[6] In addition, the Davis study came from a single EMS system while our data are from many systems across an entire state.

In anticipation of the potential for regionalization in Arizona, we evaluated the cardiac arrest patients in the SHARE database. While looking at the registry in this way does not constitute hypothesis testing, it clearly begins to build the basis for assessing the potential impact of longer transports in ROSC patients. If a strong association between TI and survival were present identifying significantly increased mortality for patients being transported longer distances, this should bring pause to those considering regionalization. While the absence of a causal association does not unequivocally prove that hospital bypass is safe, the presence of worse outcomes in patients with longer TI would lead to great caution and mandatory RCTs before any system attempted to regionalize care.

Our results failed to identify any causal association between TI and mortality. This was true of the entire group of OHCA patients as well as those for whom regionalization would be considered: patients remaining comatose after ROSC. We chose not to limit our analysis to this subset because the finding of worse mortality among the longer TI patients in the entire OHCA group would be reason to raise concern as well. The fact that there was no apparent causal relationship between TI and mortality in any group is pertinent to the discussion of regionalization.

When considering research findings in EMS, the dramatic variation in the size, deployment, administration, and funding of various systems always demands the discussion of inter-system relevance and the ''portability'' of the conclusions to other places. Clearly evidence in support of the safety of bypassing local hospitals in one system does not necessarily mean that it is safe in others. However, the fact that the OHCA cases in the Arizona registry come from 48 different EMS agencies across a vast array of system types lends credence to the applicability of our findings to other systems. The EMS agencies contributing cases to the registry include huge urban areas (population 1.32 million) to small rural communities (population 1400). Our data include patients cared for by public, private, and fire-based agencies. Davis' work reported from a single county with the agencies under the auspices of a single regional EMS authority.[10] Thus, the addition of this data from a wide variety of EMS settings adds further support to the concept that regionalization may be safe.

Limitations

The conclusions and significance of our findings are impacted by several limitations. First, although the OHCA cases in the SHARE registry are prospectively collected, this query was not an *a priori* hypothesis. Thus, the potential for impact by confounding issues is significant as with any retrospective evaluation of a data set. This was not a controlled trial but, rather, an observational analysis. In addition, the fact that data for TI was missing in 38% of cases introduces the potential for selection bias. The conclusions must also be informed by the fact that the range of the TI was not particularly broad. While there were patients in the study that had TI as long as 42 min, 95% of all cases fell within 14 min. Hence, we can make no conclusion about bypassing hospitals to go long distances for specialized care.

Conclusion

Using a statewide database, we evaluated the association between TI and outcome in OHCA patients and in the subgroup of patients with ROSC who remained comatose in the field. No causal association was identified in any cohort. While not proof, this supports the concept that a modest increase in TI for the purpose of transport to a regional cardiac center is safe. This analysis is relevant to future trials that evaluate the impact of regionalized post-resuscitation care as well as to EMS systems that consider implementing transport protocols providing for bypass of local hospitals to go to more distant specialized receiving facilities. Future investigations from much larger cardiac arrest registries and prospective, controlled clinical trials will be required to verify the safety and effectiveness of this approach to OHCA.

Conflict of interest

None.

Acknowledgement

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