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CLINICAL RESEARCH

Association of obesity with worsened prehospital cardiac arrest

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Abstract

Background. This study evaluated a potential correlation between patient age, body weight and survival from prehospital cardiac arrest, as a secondary endpoint in a study evaluating the effect of bicarbonate on survival.

Design. A prospective, randomized, double-blinded clinical intervention trial.

Methods. 874 prehospital cardiopulmonary arrest patients in a prehospital urban, suburban, and rural regional emergency medical service (EMS) area were used. This group underwent conventional Advanced Cardiac Life Support (ACLS) intervention followed by empiric early administration of sodium bicarbonate (1 mEq/L). Survival was measured as presence of vital signs on ED survival. Data was analyzed utilizing Student's *t*-test, Fisher's exact test, Chi-square with Pearson correlation and logistic regression ($p<0.05$).

Results. The overall survival rate was 13.9% (110 of 793) of prehospital arrest patients. There was no significant difference between the control and bicarbonate groups for patient age (67.7 versus 67.4 years, $p=0.769$) and body weight (87.9 versus 89.7 kg, $p=0.508$). There was no difference in outcome associated with age for non-survivors or survivors (67.3 versus 67.5 years, $p=0.943$). However, a significant difference in total body weight (TBW) was noted between non-survivors and survivors (84.9 ± 27.3 kg versus 77.3 ± 21.4 kg, $p<0.002$).

Conclusion. There is a significant adverse association between body weight and outcome, but no association between advanced age and prehospital survival.

Keywords: *Cardiopulmonary arrest, outcome, obesity, prehospital, nutrition, weight*

Introduction

The association of obesity and adverse health consequences has been well established. More chronic conditions, such as knee osteoarthritis, kidney stones, and prostate cancer are correlated with obesity [1–3]. Also, cardiac issues are involved with a clear with an adverse association between new onset atrial fibrillation and congestive heart failure [4,5].

There is also a specific association between obesity and specific comorbid conditions such as cardiovascular disease and diabetes [6]. In addition, predictive models have correlated pediatric and subsequent adult obesity [7]. A closer examination of mortality

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targets the surgical realm as an area of interest. Obesity is associated with increased mortality in office-based surgical procedures, during the ICU stay, as well as readmission and sternal dehiscence after cardiac surgery [8–10]. A single unifying hypothesis related to this accentuated mortality rate has been ascribed to left ventricular hypertrophy, systolic/diastolic dysfunction, and subsequent ventricular dysrhythmias [11–14].

The use of prehospital health care providers to intervene in acute cardiac emergencies has historically been a focus of emergency care. 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 [15]. Defibrillation was the only beneficial intervention identified, but also added a 29-minute delay to hospital arrival, suggesting the need for more streamlined care.

Later, Shuster and Chong went on to evaluate 15 prehospital studies during the early years of emergency medical care, suggesting no benefit of prehospital administration of any of a number of commonly administered prehospital medications [16]. Qualitatively, there have been few studies that have examined the use of such pharmacotherapeutic agents as albuterol, bicarbonate, bronchodilator agents, diazepam, dobutamine, dopamine, glucose, isoproterenol, naloxone, or nitrous oxide for their prehospital efficacy [17].

Paramedic effectiveness has been described for Advanced Cardiac Life Support (ACLS) intervention with a 91.7% success rate of obtaining intravenous access and 91% for intubation; however, drug administration was only consistent with 43% of resuscitation recommendations by intravenous route and 37% by endotracheal route [18]. Stricter compliance with national ACLS guidelines and facilitation that involves refresher training courses may improve effectiveness.

Four factors are related to the ability to resuscitate patients in prehospital arrest: time to starting rescue procedures, use of electrical defibrillation, accuracy of technique of basic life support (BLS), and ventilation efficacy reported according to decreasing utility [18].

Methods

This prospective, randomized multicenter clinical trial involved cardiac arrest patients encountered by paramedics (EMT-Ps) in a prehospital setting, and transported to hospitals within the study area, usually within a 5–30 minute transport radius. Inclusion criteria were subjects suffering from cardiac arrest refractory to defibrillation in which IV access was obtained. Exclusion criteria included those subjects suffering from overt respiratory or traumatic arrest, children under 18 years of age and those without IV access.

Patients received standard ACLS protocol including chest compressions, ventilation, defibrillation, epinephrine (0.01 mg/kg), atropine (0.01 mg/kg), and antiarrhythmics or pressor agents as warranted. Patients were randomized to a treatment group receiving an empiric dose of bicarbonate (Abbott, Chicago, USA) 1 ampule (50 mEq/L) early in the arrest cycle. The control group received an equal amount of normal saline in a double-blinded fashion to clarify the benefits of the osmolar load versus base deficit correction.

Routine demographic and clinical variables related to outcome were analyzed including demographics, response to bicarbonate administration, scene factors, response time, cardiopulmonary variables, procedures, and duration of arrest (Table I).

Routine cardiopulmonary variables were monitored. Neurological outcome was measured initially as the Glasgow Coma Score [19]. Patient outcome was recorded as initial emergency department survival to discharge, as a primary endpoint. Patients were enrolled under the

Table I. Prehospital correlates to survival.

Demographic	Age, Weight, Gender
Response Time	ET Arrest, ET ByCPR, ET BLS, ET ACLS, ET ROSC, ET Hosp
Interventions	Bicarbonate (Dose, Weight-based)
Scene Factor	Bystander CPR, Witnessed
Cardiopulmonary Variables	Initial Rhythm, Initial Systolic Blood Pressure (ISBP), IDBP
Procedures	Intubation, IV, Other
Duration of Arrest	Short (<5 min), Moderate (5–15 min), Long-term (>15 min)
EMS Coverage	Urban, Suburban, Rural
Past Medical History	MI, HTN, DM, CHF, COPD, CABG
Medication	Cardiac, HTN, Arrhythmia, Pulmonary, Hematologic, GI, Psychiatric, Seizure

ET, Estimated Time; ByCPR, Bystander Cardiopulmonary Resuscitation; BLS, Basic Life Support; ACLS, Advanced Cardiac Life Support; ROSC, Return of Spontaneous Circulation; MI, Myocardial Infarction; HTN, Hypertension; DM, Diabetes Mellitus; CHF, Congestive Heart Failure; COPD, Chronic Obstructive Pulmonary Disease; CABG, Coronary Artery Bypass Grafting; GI, Gastrointestina.

Doctrine of Implied Consent for the emergency use of an accepted resuscitation modality and notification was provided, if requested by family or healthcare resources.

In addition, administration of an FDA approved agent (sodium bicarbonate) in the emergency setting for moderate to prolonged arrest may be the standard of care, and in conjunction with the above conditions which are met, consent could be waived. This study was approved by the University of Pittsburgh Institutional Review Board under this rationale and was modified to address Office for Protection from Research Risk (OPRR) issues concerning 'deferred consent' [20].

Examining these same issues according to OPRR guidelines suggests further qualification to waive prospective informed consent according to the second waiver condition of 45 CFR 46.116 section D [21].

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 could not practicably be carried out without the waiver or alteration.
4. Whenever appropriate, the subjects were provided with additional information after participation.

Numerical data was represented as mean and standard deviation with Student's *t*-test, Fisher's exact test, Chi-square with Pearson correlation tests utilized for logistic regression intergroup comparison ($\alpha<0.05$) (SPSS/PC+®, Chicago, IL). The study results were examined by the investigators at three-month intervals (or 25% of projected patients) to verify early trends and outcomes with capability of later modification.

The sample size of 1,000 was sufficient to delineate a 50% difference in survival and neurological outcome at 80% power and a 95% confidence interval between control and treatment groups. This estimate was based on a 12% rate of return of spontaneous circulation (ROSC) in prehospital arrests. This was a single step emergent intervention excluding the need for stopping rules.

Results

The overall survival rate was 13.9% (110 of 793) of prehospital cardiac arrest patients (Figure 1).

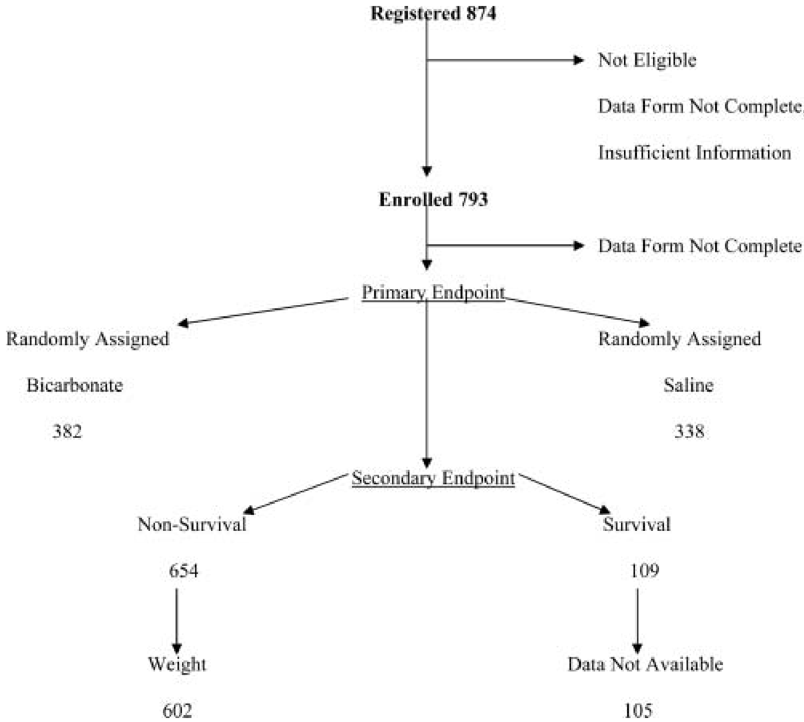

Figure 1. Trial profile.

The study groups were analyzed to examine for discrepancies in the per-experimental groups. We found no significant difference between the control and bicarbonate groups for patient age (67.7 versus 67.4 years, p=0.769) and body weight (87.9 versus 89.7 kg, p=0.505).

There was no difference in outcome associated with age for nonsurvivors versus survivors (67.3 ± 14.9 versus 67.5 ± 15.2 years, p=0.943) (Table II). However, a significant difference in total body weight was noted between nonsurvivors (84.9 ± 27.3 kg) and survivors (77.3 ± 21.4 kg, p=0.002) (Table III).

Discussion

Prehospital predictors of outcome may potentially be inferred by the analysis of animal experimental data. Angelos et al. evaluated a ten-minute ventricular fibrillation (VF) and five-minute Basic Life Support (BLS) resuscitation model to identify improved coronary

Table II. Demographic variables correlated to survival.

	Nonsurvival	Survival	Significance
Age (years)	67.34 ± 14.88	67.45 ± 15.22	0.943
Patients	654	109	
Weight (kg)	84.86 ± 27.25	77.32 ± 21.39	0.002
Patients	602	105	

Table III. Demographic information.

	Cumulative	Control	Bicarbonate	Significance *p* value
Age (years)	67.56 ± 15.09(3–101)	67.68 ± 14.96	67.37 ± 15.29	0.769
Patients	853	373	418	
Weight (kg)		87.87 ± 33.39	89.73 ± 42.74	0.508
Patients		346	395	

perfusion in the normal neurological outcome group as an independent predictor of favorable outcome [22]. The author has performed a similar trial in brief (five-minute), moderate (ten-minute), and prolonged (15-minute) canine VF model to also identify improved coronary (COPP) and systemic (MAP) perfusion pressure as favorable outcome predictors associated with improved survival and neurological outcome [23].

Brison et al. published a demographic analysis of the cardiac resuscitation experience of 1510 cardiac arrest patients where 92.1% of patients were 50 years of age, 68.3% were male and 79.6% of arrests occurred at home [24]. The average ambulance response time of witnessed events was 7.8 minutes with an overall survival rate of 2.5%. Factors predicting survival include age, ambulance response time, whether CPR started before ambulance arrival, but interestingly was not related to early defibrillation.

Tresch evaluated a population of 381 cardiac arrest patients comparing older and younger (<20 years) cohorts, who have undergone paramedic witnessed cardiac arrest [25]. The elderly patient cohort more commonly had a past history of heart failure (25 versus 10%), were more commonly taking digoxin (40 versus 20%) and/or diuretics (35 versus 25%), and were more likely to complain of dyspnea (53 versus 40%). Younger patients were more likely to complain of chest pain (27 versus 13%) and presented in ventricular fibrillation (42 versus 22%). Interestingly, the patients' chief complaint correlated with initial rhythm where 68% of those with chest pain demonstrated a ventricular fibrillation event compared to 21% of those with dyspnea. Although there were equivalent initial resuscitation rates in the elderly, their survival to discharge was decreased comparatively (24 to 10%).

Survey data offered by Ng et al. concerning 105 younger (1–39 years) arrest patients found a male predominance (62%), occurring secondary to cardiac disease (38%) due to atherosclerotic heart disease in 50% and secondary toxic exposure in 21% [26]. The most common presenting rhythm was ventricular fibrillation (VF) (45%) associated with a 48% resuscitation rate with over 28% of post-resuscitation patients progressing to long-term survival. Favorable outcome was predicted by the arrest being witnessed, or associated with primary cardiac dysrhythmia; while asystole was a negative prognostic indicator and age, sex, race, bystander CPR, and paramedic response time were not significant prognostic factors affecting long-term survival.

Similar survey data from Valenzuela et al.'s 372 prehospital patient study demonstrates a 20% survival rate to hospital admission and 6% survival to discharge [27]. This rate was improved to 26% for hospital admission and 10% for hospital discharge in witnessed events, and 38% and 15% respectively for witnessed ventricular fibrillation. Bonnin and Swor evaluated a 181 patient group where 6% (10) who failed prehospital resuscitation survived to hospitalization, but only 0.6% (1) were discharged neurologically intact, with gender as the only predictive correlate [28].

The outcome of cardiac arrest in the elderly has been suggested as being associated with worsened survival. Murphy et al. evaluated 503 elderly patients with in-hospital arrest demonstrating 22% initial and 3.8% survival to discharge [29]. Likewise, Hallstrom et al. found an inverse association between age and survival [30].

Interestingly, we found there to be no age relationship in our arrest cohort with a mean age range for survivors of 67.3 years and nonsurvivors of 67.5 years. Perhaps we are prone to β-error as our study sample size was insufficient to prove a relatively small clinical difference. The prevalence of obesity, which was defined as body mass index (BMI) >40 or weight >100% above ideal body weight, may be as high as 30%. In addition, it is predicted to continue to increase in the future due to poor cardiopulmonary reserve [31,32]. In addition to increasing prevalence, obesity is associated with increased morbidity and mortality.

Manson et al. reported from a study of 115,886 women in a prospective cohort analysis to define an increase in all categories of coronary artery disease (CAD) based on an increased weight index [33]. Jousilahti et al. found obesity to be an independent risk factor for coronary heart disease mortality. This risk is higher for men than women and is probably mediated through other known cardiovascular risk factors [34].

The molecular basis of obesity has been studied as it relates to medical outcome. There is an association between leptin and BMI resulting in worsened hypertension [35]. The presence of excess polyunsaturated N-3-fatty acids (PUFA) in the diet is associated with reduced murine resistance to infection [36]. The suggestion is that the western diet with a 20–25 fold ratio of omega 6/3 PUFA causes the release of inflammatory arachidonic acid metabolites (leukotrienes and prostanoids) [37].

Clearly, there is an adverse effect of a dietary excess of monounsaturated fatty acids (MUFA), and not just the adiposity alone responsible for adverse outcomes [38]. In separate trials Garaulet and Paschos correlated obesity, defined as BMI $>27\,kg/M^2$, with excess MUFA ingestion as a proportion of total nutrient intake, while ingestion of long chain N-3 PUFA may be protective through their anti-inflammatory effects [39,40].

The interface between antioxidant vitamins and coronary heart disease risk has been well described with both protective and adverse effects of vitamin C [41,42]. Vitamin C supplementation has also been associated with a more favorable clotting profile, decreased cell apoptosis, and improved free radical clearance on a mechanistic scale [43–45].

In our study, the association between increased body weight and the nonsurvival cohort was well defined with an 8 kg increase in mean body weight associated with worsened outcome compared to survivors. Although no absolute cut-off was noted, the linear relationship between excess body weight and mortality was well defined.

However, this study was not designed to elicit the primacy of this relationship so other variables may be implicated, as well as co-variables related to the poor cardiac reserve of obese patients in general.

Sodium Bicarbonate Study Group

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