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Cardiocerebral Resuscitation: An Approach to Improving Survival of Patients With Primary Cardiac Arrest

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Abstract

Out-of-hospital cardiac arrest (OHCA) is a major public health problem. In the United States, OHCA accounts for more premature deaths than any other cause. For over a half-century, the national "Guidelines" for resuscitation have recommended the same initial treatment of primary and secondary cardiac arrests. Using this approach, the overall survival of patients with OHCA, while quite variable, was generally very poor. One reason is that the etiologies of cardiac arrests are not all the same. The vast majority of nontraumatic OHCA in adults are due to a "primary" cardiac arrest, rather than secondary to respiratory arrest. Decades of research and ongoing reviews of the literature led the University of Arizona Sarver Heart Center Resuscitation Research Group to conclude in 2003 that the national guidelines for patients with primary cardiac arrest were not optimal. Therefore, we instituted a new, non-guidelines approach to the therapy of primary cardiac arrest that dramatically improved survival. We called this approach cardiocerebral resuscitation (CCR), as it is the heart and the brain that are the most vulnerable and therefore need to be the focus of resuscitation efforts for these patients. In contrast, cardiopulmonary resuscitation should be reserved for respiratory arrests. Cardiocerebral resuscitation evolved into 3 components: the community, with emphasis for lay individuals to "Check, Call, Compress" and use an automated external defibrillator if available; the Emergency Medical Services, that emphasizes delayed intubation in favor of passive ventilation, urgent and near continuous chest compressions before and immediately after a single indicated shock, and the early administration of epinephrine; and the third component, added in 2007, the designations of hospitals in Arizona that request this designation and agree to receive patients with return of spontaneous circulation following OHCA and to institute state-of-the-art postresuscitation care that includes urgent therapeutic mild hypothermia and cardiac catheterization as a Cardiac Receiving Center. Each component of CCR is critical for optimal survival of patients with primary OHCA. In each city, county, and state where CCR was instituted, the result was a marked increase in survival of the subgroup of patients with OHCA most likely to survive, for example, those with a shockable rhythm. The purpose of this invited article on CCR is to review this alternative approach to resuscitation of patients with primary cardiac arrest and to encourage its adoption worldwide so that more lives can be saved.

Keywords

cardiac arrest, passive ventilation, ventricular fibrillation, prevention

Introduction

Cardiovascular disease is the leading cause of death in almost all industrialized nations of the world.[1-3] Unfortunately, the first sign of cardiovascular disease is often the last, as nearly half of all cardiovascular mortality is from sudden cardiac death—the majority occurring out of the hospital.[4,5] The average age of individuals with out-of-hospital cardiac arrest (OHCA) in the United States is the mid 60s. After the age of 40, an American male has an 1 in 8 chance of having sudden cardiac death.[6] In individuals younger than 40 years of age, the majority of OHCAs are genetic in origin, and these individuals and their relatives should be referred for cardiovascular evaluation and genetic counseling in specialized centers. But in individuals older than the age of 40, the most common cause of OHCA is coronary artery disease.[7,8] To prevent most cardiac arrest in adults, one needs to aggressively

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treat the risk factors for coronary artery disease. To improve survival of those who have primary cardiac arrest, cardiocerebral resuscitation is recommended.

Survival From Primary Cardiac Arrest Was Unchanged for Decades

In spite of the first "Standards," then "Standards and Guidelines" then "Guidelines" and then numerous updates of the national "Guidelines" for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC), the published survival rate of patients with OHCA averaged only 7.6% and was unchanged over 3 decades.[9] However, reports that emphasize overall survival, as recommended in "Utstein 2," are not helpful since the majority of individuals with OHCA present with asystole or pulseless electrical activity (PEA), rhythms that rarely respond to even the most advanced therapy.[10] In contrast "Utstein 1" recommended reporting survival of those patients with a shockable rhythm, for example, ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT).[11] The survival rate of these individuals provides a better indicator of the effectiveness of one's Emergency Medical Services (EMS) system—a figure that all interested in OHCA should know. Unfortunately currently, many journals accept Utstein 2 recommendations and only emphasize overall survival. The survival of patients, with the greatest chance of survival, for example, those with primary cardiac arrest, is often not even mentioned in the abstract.[12]

But even when one focused on OHCA with a shockable rhythm, the published survival rate in the United States averaged 17.7% and was unchanged for decades.[13] Unfortunately, even these averages are deceiving as there are disparate survival rates of patients with OHCA due to VF treated according to national American Heart Association (AHA) guidelines in different communities. For example, the Resuscitation Outcomes Consortium analyzed the survival of patients with OHCA who were treated according to the 2005 guidelines and reported that survival varied 5-fold.[14] In this study, the median survival of VF arrest was 22% but varied from 7.7% to 39.9%.[14]

Everyone would like to have the excellent survival rates that have been reported from locations such as Seattle or Northern Netherlands, where the incidence of dispatch assisted bystander CPR is high and EMS response times are short.[15,16] As one is making national and international guidelines for CPR and ECC, who do you want in charge of setting the guidelines? The logical choice is individuals from areas that have the best survival rates. But as noted previously, following the 2005 national guidelines, the survival rates were quite variable.[14] This important publication emphasizes that "one size does not fit all."

Different Approaches Are Needed for Primary and Secondary Cardiac Arrests

Primary cardiac arrest is most often due to a life-threatening ventricular arrhythmia, where breathing was normal or near normal right up to the time of the arrest. Consequently, the arterial blood oxygen saturation at the time of a primary cardiac arrest is near normal. In marked contrast, in patients with secondary cardiac arrest, due to drowning or other causes of respiratory insufficiency such as drug overdose, the arterial blood becomes significantly desaturated and the heart does not stop until several minutes later.[17]

Cardiocerebral Resuscitation (Overview)

Cardiocerebral resuscitation (CCR) is indicated for primary cardiac arrest; the most common cause of OHCA. Cardiocerebral resuscitation originally had only 2 components.[18,19] With the designation of some hospitals in Arizona as cardiac receiving centers, CCR evolved into 3 components (Figure 1A).[20]

The first is the *community* component that emphasizes bystander recognition of primary cardiac arrest, calling to activate the EMS, and beginning chest compression-only "CPR" (CO-CPR). The Sarver Heart Center's tagline for the community component of CCR is the 3 Cs: "Check, Call, Compress"![21] The second is EMS approach to patients with primary cardiac arrest that also dramatically changed (Figure 1B). The third is the hospital component. In Arizona, hospitals that provide optimal care of patients with return of spontaneous circulation (ROSC) following OHCA are designated as "Cardiac Receiving Hospitals."[20]

Community Component of CCR

Critical to survival is the prompt recognition of OHCA. How should we teach bystanders to recognize primary cardiac arrest? A primary cardiac arrest is, "an unexpected witnessed (seen or heard) collapse in an individual who is not responsive." Of note is the fact that this description does not mention arterial pulsations or the presence or absence of respirations. Except in newborns, gasping or agonal breathing is a common sign of cardiac arrest, occurring in slightly more than 50% of patients with primary cardiac arrest.[22-25] Unfortunately, many bystanders, including physicians, mistake gasping for breathing and delay the initiation of bystander CPR until gasping stops, minutes after VF arrest.[25] Mammals are the only species that gasp when we are born and gasp when we die. Gasping must be emphasized as a sign of cardiac arrest.[21] Gasping is a primitive form of respiration that is probably initiated in the brain stem. If adequate chest compressions are promptly initiated, the patient will continue to gasp.[23]

Chest Compression-Only CPR Recommended

Cardiocerebral Resuscitation advocates CO-CPR for primary cardiac arrest. The reason for this change was that the requirement of mouth-to-mouth (MTM) ventilation as the initial step of bystander resuscitation prevented many, including professionals, from initiating bystander CPR.[26-29] In our animal experimental studies of the 1990s, survival was better with CO-CPR compared to no CPR for 8 to 12 minutes to simulate the lack of bystander CPR.[18] We also found that survival was similar to either CO-CPR or the "2000 Guidelines for CPR,"

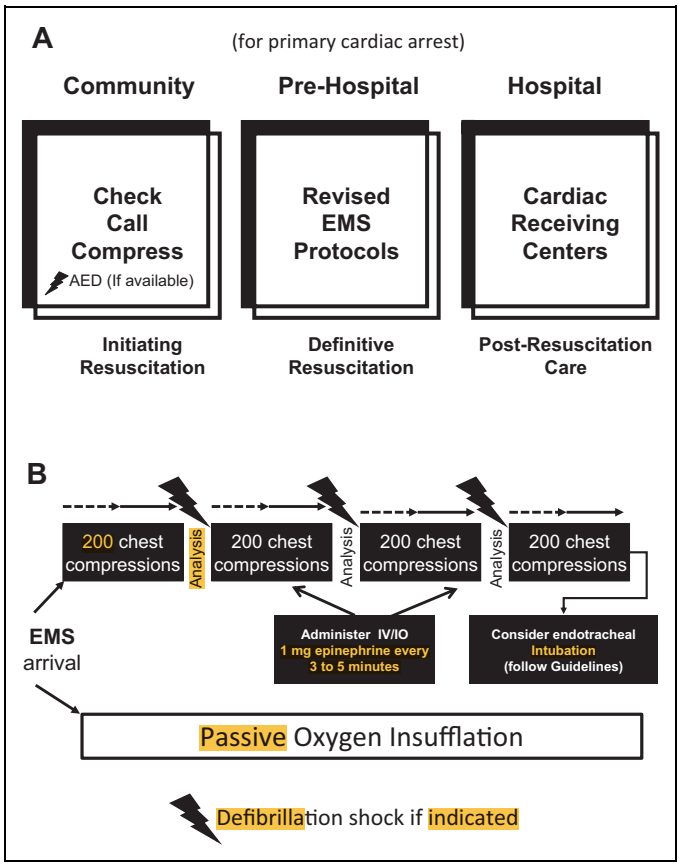

Figure 1. A, The 3 major components of cardiocerebral resuscitation: the community component initiates resuscitation efforts and has 3 major steps for all bystanders. They are to "Check" to ascertain that the patient is in cardiac arrest, "Call" to the dispatch center, and "Compress" to initiate chest compression-only cardiopulmonary resuscitation (CPR). If an automated external defibrillator (AED) is readily available, it should be used. The prehospital component is a revised emergency medical services (EMS) component, usually where definitive therapy occurs. The hospital component in Arizona is a designation that is given to a hospital that commits to 24/7 provision of optimal care of the patient with ROSC. In Arizona, these hospitals are designated as a Cardiac Receiving Center. **B**, This is a graphic presentation of the Emergency Medical Services component of cardiocerebral resuscitation. It emphasizes delayed intubation in favor of passive ventilation, a series of continuous chest compressions before and immediately after a single indicated shock, and the early administration of epinephrine.

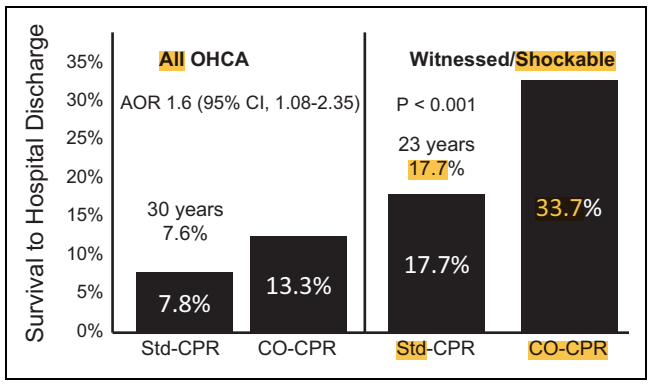

Figure 2. Survival to hospital discharge of patients out-of-hospital cardiac arrest (OHCA) in Arizona from January 1, 2005, to December 31, 2009, a time when chest compression-only CPR was advocated and taught to the public. The survival of patients who received "Guidelines" or standard CPR (Std-CPR), for example, mouth-to-mouth ventilations plus chest compressions, was 7.8%, close to the 30-year average survival of such patients reported survival rate of 7.6%. In contrast, patients who received chest compression-only CPR (CO-CPR) had an overall survival rate of 13.3%. Patients with a witnessed arrest and a shockable rhythm upon arrival of the Emergency Medical System, who were treated by bystanders with Std-CPR (eg, mouth-to-mouth ventilations plus chest compressions) was 17.7%, the exact percentage of the average reported survival of patients with OHCA due to ventricular fibrillation reviewed by Rae and associates. In contrast, patients with a witnessed, shockable OHCA was 33.7% with CO-CPR. The odds ratio strongly favored cardiocerebral resuscitation. CPR indicates cardiopulmonary resuscitation.

which not only recommended "rescue breathing" as the first step of bystander CPR but also recommended interrupting every 15 chest compressions for 2 quick breaths of 2 seconds each for rescue breathing.[18] Then a little known but landmark study by Assar, Chamberlain, and associates, including Karl B. Kern, MD, from the University of Arizona Sarver Heart Center Resuscitation Research Group, documented that lay individuals, recently certified in basic life support, interrupted chest compression an average of 16 seconds to deliver the decades old recommendation of "rescue breaths" between each set of chest compressions.[30] With this knowledge, we compared survival in our realistic (nonparalyzed) swine model of OHCA between chest CO-CPR and realistic CPR and found that survival was dramatically better with CO-CPR.[31,32] In 2008, the AHA published a "Call to Action" advisory, in which they advised lay bystanders to provide "Compression Only CPR," using their new term "Hands-Only CPR."[33]

In the event that an automated external defibrillator (AED) is available, the bystander is to open the unit and follow its automated instructions. Unfortunately, AEDs are not often readily available, and if available, most are not programmed to give instructions in CO-CPR. There is no doubt that AEDs save lives. Of note is a recent report by Iwami and associates from Japan that survival was even better when CO-CPR was an adjunct to CO-CPR.[34]

Survival Improved by Teaching and Advocating CO-CPR for Primary Cardiac Arrest

After Dr Bentley J. Bobrow, Medical Director of the Bureau of Emergency Medical Services and Trauma System at the Arizona Department of Health Services, established an Arizona statewide database in 2004 that tracked the survival of patients with OHCA, we initiated an educational campaign in Arizona to advocate CO-CPR for patients with primary OHCA.[12] As shown in Figure 2, survival of patients with witnessed OHCA who received CO-CPR was significantly better than those who received the standard AHA/European Resuscitation Guidelines (ERC) recommended therapy.[12] Of interest is that only a

minority of individuals with noncardiac arrest received CO-CPR.[35] In Arizona, the public was generally capable of recognizing respiratory arrest, where chest compressions and assisted ventilations were recommended.

Compression-Only Bystander CPR Improved Survival in Japan

Iwami and associates analyzed the outcome of 1376 individuals in a prospective, nationwide population-based cohort study of OHCA individuals in Japan, in which the bystander performed CPR and used an AED.[34] Therefore, these patients all had primary OHCA and a shockable rhythm; a subset of patients with OHCA who were most likely to survive. The patients who received CO-CPR had a 1-month neurological favorable survival rate of 40.7%, compared with 32.9% for those who received MTM ventilation plus chest compressions.[34] These results were even more significant for in Japan, as these authors reported that 1.6 million citizens participated in bystander CPR training each year, training sessions that taught MTM[36] ventilation plus chest compressions and AED use.[34] Because of the large database of the "All Japan Utstein Registry," there have been a number of publications from Japan reporting survival of patients with OHCA. In Japan, bystanders received dispatcher-CPR instructions with CO-CPR or 15:2 compressions to ventilations before January 1, 2006, and instructions in CO-CPR or 30:2 CPR between January 1, 2006, and March 31, 2007. After March 31, 2007, all bystanders received dispatch-assisted CPR with either CO-CPR or 30:2 CPR (K. Nagao, MD, Personal communication, March 2013). The proportions of dispatcher-CPR instructions for bystander-witnessed OHCA due to cardiac etiology (n = 115 158) increased from 9.4% in 2005 to 24.0% in 2010, while instruction in conventional CPR decreased from 10.2% to 6.5% during this same time period (K. Nagao, MD, personal communication, March 2013).

The 2005 and 2010 International CPR guidelines recommended that citizens previously trained in CPR provide 30:2 CPR but that dispatchers should provide telephone instruction in CO-CPR for citizens not trained in CPR.[36,37] The Japanese Circulation Society Resuscitation Science Study Group subsequently evaluated 78 150 patients receiving bystander CPR.[38] The prevalence of dispatcher-assisted CPR instruction increased year by year, contributing to an overall increase in chest compression-only bystander CPR from 20.6% to 35.0%. They reported that patients receiving CO-CPR had a more favorable neurological outcome than those receiving standard CPR in the whole cohort (adjusted odds ratio [OR], 1.09; 95% confidence interval [CI]: 1.00-1.18) and in the subgroup with cardiac etiology (adjusted OR, 1.12; 95% CI: 1.02-1.22). The addition of rescue breathing provided no neurological benefit in the noncardiac etiology subgroup.[38]

Advanced Cardiac Life Support Protocol for CCR

The EMS is a critical component of CCR (Figure 1A and B). The community and the EMS components of CCR deserve emphasis, for in the majority of patients with OHCA, the battle for life or death is won or lost in the field, long before the patient is ever seen by a physician.

The EMS component of CCR emphasizes minimally interrupted chest compressions.[18,39,40] It became obvious that during cardiac arrest, chest compressions are the patient's heartbeat and that anything that interrupts or delays continuous chest compressions is deleterious.[41,42]

Chest Compressions Before Defibrillation for Prolonged VF Arrest

Obviously, if the paramedics or EMS personnel witness the arrest or if there is optimal continuous chest compressions in progress when the EMS arrive, the protocol is immediate defibrillation. In patients with primary cardiac arrest, the EMS protocol of CCR emphasized prompt initiation of 2 minutes of continuous optimal (rate, depth, and release) chest compressions at a metronome-guided rate of 100 per minute before and immediately after a single indicated direct current (DC) shock (Figure 1B).

The recommendation of *chest compression prior to defibrillation* during untreated VF arrest came from a meeting under the aegis of the Resuscitation Council of the United Kingdom in 2002, involving a small group of experts from Europe and Dr Karl B. Kern and Gordon A. Ewy from the United States. On that trip, we visited the laboratory of Dr Stig Steen who demonstrated, in open-chest swine, that during the first few minutes following the onset of untreated VF, the fibrillating right ventricle enlarged and the fibrillating left ventricle gradually became smaller as the blood in the arterial system shifts into the lower pressure venous system.[43] This phenomenon is the volume expression of the classic pressure experiments of Guyton who reported decades before that following the onset of VF arrest, the arterial pressure falls and the venous pressure rises until the pressures became nearly equal; the pressure he designated as the mean circulatory filling pressure.[44] While impressed with Dr Steen research, we wondered if the same heart volume changes occurred in the closed-chest swine. Years later, another member of the University of Arizona Sarver Heart Center Resuscitation Group, Vincent Sorrell, MD, led our experiment that showed by magnetic resonance imaging that the same phenomenon occurred in the closed-chest swine model following the introduction of VF arrest.[45] In fact the right ventricle enlarged significantly within 1 minute of VF arrest.[46]

We were also influenced by another important finding in our research laboratory. As is well known, in untreated VF arrest, there was a gradual decrease in the amplitude of the VF waves on the electrocardiogram. We found that the amplitude of VF on the electrocardiogram could be increased by chest compressions that were instituted relatively early and that this intervention increased survival.[47] We assumed that perfusing the heart restored energy stores, for if the fibrillating heart is perfused, it can defibrillate for days!

Since EMS personnel historically arrived at the side of a patient with OHCA who had not received any or optimal bystander CPR, we recommended that they first initiate chest compressions. Our choice of 200 chest compressions before defibrillation was not only influenced by Dr Steen work but also by the published information on humans. The 2 minutes of chest compression was a compromise between the 90 seconds of chest compression prior to defibrillation that Dr Leonard Cobb of Seattle recommended for their paramedics and the 3 minutes that Dr Lars Wik recommended for their paramedics prior to defibrillation.[48,49]

It turns out that 2 minutes of CPR prior to defibrillation was shown to be the optimal duration in one of the Resuscitation Outcomes Consortium (ROC) studies.[50] A plot of the probability survival of 1638 patients with OHCA against the duration of chest compressions provided by EMS prior to defibrillation of VF/VT resulted in a bell-shaped curve showing survival peaked at 2 minutes.[50] A subsequent randomized controlled trial by the ROC study group showed no difference in survival, when they did not plot the bell-shaped curve, but just compared survival of those who received 30 to 60 seconds of chest compression or 180 or more seconds of chest compression before defibrillation.[51]

Minimizing the Delay Between Chest Compressions and Shock Is Important

Dr Max Weil laboratory and others reported that the interruption of chest compressions for more than 15 seconds before each shock compromised the outcomes of CPR and increased the severity of postresuscitation myocardial dysfunction.[52] This and other studies lead to the common practice of charging the defibrillator during the last few seconds of the preshock chest compressions and assuring that those involved in the resuscitation procedure are "all off," as the defibrillator shock is delivered, followed immediately by the command of "back on" to direct the prompt onset of postshock chest compressions.

Why 2 Minutes of Chest Compressions Immediately After a Defibrillator Shock?

The recommendation for resuming chest compressions immediately after a defibrillation shock without an analysis of the electrocardiogram or searching for a pulse is another important aspect of CCR.[18,19] It was a common scenario for medical professionals, upon seeing a "QRST" complex on the electrocardiogram monitor after the DC shock, not to restart chest compressions but to search for a pulse, not realizing that PEA is common follow defibrillation of prolonged VF.[53] But without chest compressions immediately following the shock, the electrocardiogram will deteriorate, often to heart block or asystole. Chest compressions should be initiated immediately post-DC shock to perfuse the heart and increase the likelihood that it will be able to generate adequate arterial pressures.[18]

Passive Ventilation Advocated During Early Minutes of Resuscitation in Patients With Primary Cardiac Arrest

The CCR protocol prohibited early endotracheal intubation (ETI) for 2 reasons. The first is that all too often ETI results in excessive delays or interruptions of chest compressions and the second is to prevent the hemodynamic deleterious effects of positive pressure ventilation during resuscitation efforts and to prevent "death by hyperventilation."

Although well known for decades by those of us who responded to cardiac arrests in hospitals, Wang and associates were the first to report on the actual delays and or interruptions in chest compressions occasioned by attempts of ETI by EMS personnel.[54] Wang and associates reported on the durations of interrupted of chest compressions for ETI in 100 patients with OHCA.[54] The median duration of interruptions of chest compressions was 47 seconds, one-third exceeded 1 minute and one-fourth exceeded 3 minutes.[54] These durations of no cerebral blood flow in a cardiac arrest practically preclude neurologically intact survival. Granted there are systems, like in Seattle, where highly trained paramedics can most often accomplish ETI without interruptions of chest compressions, but this skill appears to be an exception rather than the rule.[55]

Another major concern for patients in cardiac arrest treated by EMS using either ETI or bag-valve-mask (BVM) ventilation was "death by hyperventilation."[56,57] Aufderheide and associates pointed out the risks of hyperventilation—a previously common problem occasioned by the excitement of the resuscitation effort.

Positive Pressure Ventilation Not Optimal During Cardiac Arrest

During normal ventilation, air enters the lungs in response to the negative pressure generated by the inspiratory phase of respiration. This negative pressure also augments venous return to the chest. In contrast, positive pressure ventilation during cardiac arrest, especially when excessive and fast, increases intrathoracic pressures, decreases venous return, and thus forward blood flow. In addition, increased intrathoracic pressures are reported to increase intracerebral pressure.[58-60] These deleterious effects of hyperventilation can be prevented by passive oxygenation.[18]

When CCR was first introduced statewide in Arizona, Dr Bobrow was concerned that if the emergency medical technician/paramedics were told that they should not intubate, also use only passive ventilation, that they might not embrace CCR at all. Accordingly, although passive ventilation was recommended, he allowed assisted ventilation by BVM. When the results of CCR in Arizona were subsequently analyzed, survival-to-hospital discharge was 26% in patients ventilated with BVM and 38% in those provided passive ventilation.[59] This obviously was not a randomized control trial but provided more support for the use of passive ventilation for patients with primary cardiac arrest.

Are Advanced Airways Associated With Impaired Outcomes?

Investigators from Japan recently reported that advanced airways were associated with an impaired outcome.[60] In an observational study from the All-Japan Utstein Registry, Hasegawa and associates reported on the evaluation of the 281 522 patients with OHCA who were treated with ETI were less likely to survive than the 367 837 patients who were treated with bag-mask ventilation.[60] Doctors Berg and Bobrow recently pointed out that these findings are consistent with several previous observational studies from other countries.[61]

Cardiocerebral resuscitation protocol that delayed advanced airway in favor of passive ventilation improved survival when compared to the survival in the EMS areas where they followed the 2000 national and international guidelines for airway management. In addition, both Hanif et al in 2010 and Egly et al in 2013 reported better survival in patients without intubation than those who received ETI.[62,63]

Epinephrine Therapy During Primary Cardiac Arrest

Cardiocerebral resuscitation advocates the early administration of epinephrine (Figure 1A). This recommendation was based on early experiments in animals with VF arrest, where survival was improved with the early administration of epinephrine.[64] This recommendation was supported by our more recent animal studies that found survival was improved when epinephrine was administered at a reasonable time period following the primary VF arrest.[65] The first publicized randomized controlled double-blind trial of epinephrine versus placebo for OHCA in humans, when analyzed by a Bayesian interpretation of the results, suggests a beneficial effect of epinephrine (CI 2.1 with 95% CIs of 0.8-6.6).[66,67] In another study from Japan, investigators found improved survival in patients with OHCA who received epinephrine by EMS providers.[68] Thus, in 2 published randomized controlled trials of epinephrine versus placebo for patients with OHCA, the survival was better in the group who were given epinephrine. Based on our findings in our experimental laboratory and these 2 randomized studies in humans, we continue to recommend early epinephrine.[64] To administer early epinephrine, intraosseous administration is recommended.[65] There have been studies in humans that have questioned the value of epinephrine, but in these studies, epinephrine was administered so late in the resuscitation effort that one has to conclude that their findings were not universally applicable.[69]

Survival With CCR Versus 2005 National and International Guidelines

The question was how does survival of patients with OHCA treated with CCR compare to survival of patients treated with the 2005 update of the national and international guidelines for CPR and ECC? A systematic review and a meta-analysis of quality studies were carried out to determine whether the use of CCR or the 2005 AHA/ERC improved survival over that obtained when these same units followed the 2000 AHA/ERC guidelines. The results are shown in Figures 3 and 4.[70]

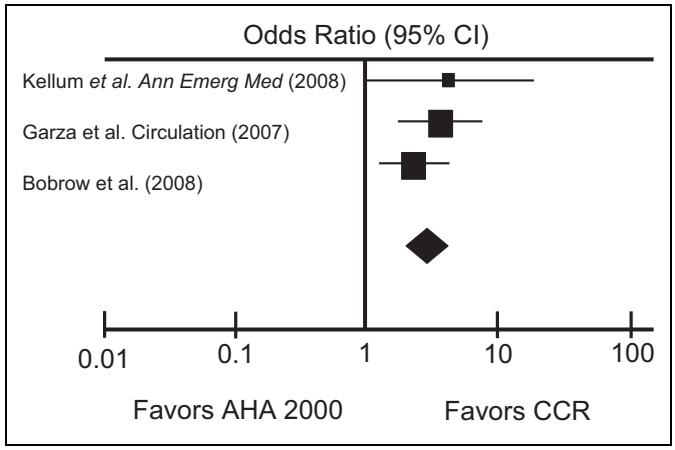

Figure 3. A forest plot of the odds ratios for survival of patients with witnessed out-of-hospital cardiac arrest due to ventricular fibrillation treated with cardiocerebral resuscitation (CCR) versus the survival of their patients when these same Emergency Medical Services followed the American Heart Association (AHA) 2000 Guidelines. The overall odds ratios were not different.

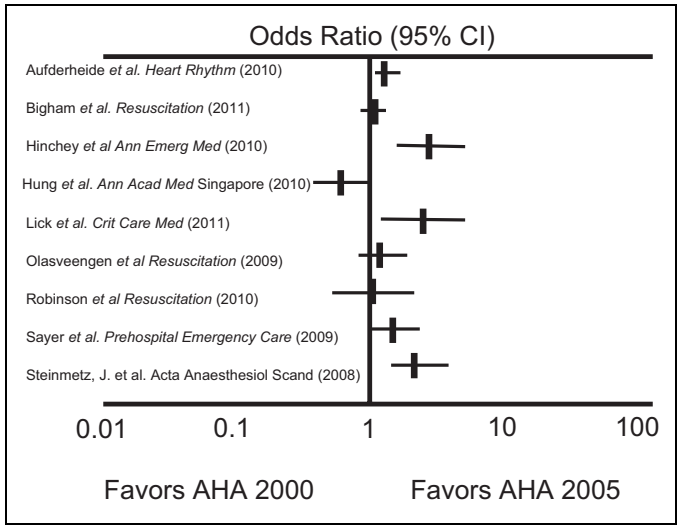

Figure 4. A forest plot of the odds ratios for survival of patients with witnessed out-of-hospital cardiac arrest and ventricular fibrillation treated with the 2005 Guidelines versus the survival of their patients when these same Emergency Medical Services followed the American Heart Association 2000 Guidelines.

All 3 reported studies using CCR demonstrated significantly improved survival compared to the use of AHA 2000 guidelines, as did 5 of the 9 studies using AHA/ERC 2005 Guidelines for CPR and ECC.[70] Pooled data demonstrated that the use of a CCR protocol has an unadjusted OR of 2.26 (95% CI: 1.64-3.12) for survival-to-hospital discharge among all cardiac arrest patients. Among witnessed VF/VT patients, CCR increase survival by an OR of 2.98 (95% CI: 1.92-4.62; Figure 3).[70] Studies using AHA 2005 Guidelines showed an

overall trend toward increased survival but significant heterogeneity existed among these studies, as shown in Figure 4.[70]

Comparisons of survival of patients with primary cardiac arrest and a shockable rhythm between CCR and 2010 AHA/ERC guidelines have not, to this author's knowledge, been studied. However, the 2010 AHA/ERC guidelines were little changed from the 2005 guidelines.

Cardiac Receiving Centers

The hospital (Figure 1A) is the third component of CCR. In the early 2000s, a variety of reports established the fact that aggressive in-hospital therapy of patients with ROSC following OHCA improved survival.[71,72] These reports were supported by studies that showed the benefits of therapeutic mild hypothermia (TMH) and urgent cardiac catheterization.[72,73] In 2007, the Arizona Department of Health Services under the direction of Bentley J. Bobrow, Medical Director, Bureau of Emergency Medical Services and the University of Arizona Sarver Heart Center Resuscitation group, embarked on a program of designating hospitals as Cardiac Receiving Centers.[20] To be designated as a Cardiac Receiving Center, a hospital had to commit to "24/7" provision of (1) TMH, (2) urgent cardiac catheterization and appropriate interventional therapy, (3) delaying "termination of care" for at least 72 hours after therapeutic hypothermia, (4) a protocol to address organ donation, (5) commitment to teach CPR to their surrounding community, and (6) a commitment to submission of data (1 page) to The Save Hearts in Arizona Registry and Education (SHARE) program (azshare.gov) for the 6 months before instituting the SHARE protocol and biyearly thereafter.[20] However, not all hospitals could commitment to providing advanced therapy for patients with ROSC following cardiac arrest. The State EMS Council developed and approved a prehospital protocol that allowed EMS personnel to bypass the nearest local hospitals and transport eligible patients (comatose patients with ROSC) to Cardiac Receiving Center hospitals with a maximal transport interval not to exceed 15 minutes. This time limit was arrived at after analysis of statewide OHCA transport interval data.[74]

Based on the classic studies published in the *New England Journal of Medicine* of therapeutic hypothermia, the recommended target temperature goal was 32°C to 34°C.[75] The targeted temperature management (TTM) trial by Nielsen et al compared 2 target temperatures, both intended to prevent fever.[76] They randomly assigned 950 unconscious adults after OHCA of presumed cardiac cause to a TTM at either 33°C or 36°C.

Their trial showed no difference in survival of patients with ROSC after cardiac arrest treated with a therapeutic hypothermia target of 33° versus 36°. At the 180-day follow-up, 54% of the patients in the 33°C group had died or had poor neurologic function, compared with 52% of patients in the 36°C group.[76] This trial suggests that patients intolerant to the colder temperature because of increased bleeding, bradycardia, or marked "QT interval" prolongation on their electrocardiogram should be managed with a temperature goal of 36°C.

Improving Survival of Patients With OHCA

The problem is that the vast majority of physicians have no idea what the survival rate of patients with OHCA is in their area. This needs to change if major progress is to be made. Unfortunately, following the national and international "Guidelines" is no guarantee that your EMS system is as effective as it should be.

An common approach to improving outcomes of any endeavor is called continuous quality improvement (CQI); a concept where one measures outcomes, makes reasonable changes, and measures the results.[21] The survival rates of patients with OHCA in VF arrest between 1977 and 2003 in Tucson, Arizona, were extremely poor and unchanged despite instituting each national guideline update.[18,19,21] Based on The University of Arizona's Sarver Heart Center's Resuscitation Research Group's decades of research, first into defibrillators and defibrillation, and then our animal studies on the effects of drug therapy on survival from primary cardiac arrest, our research evolved into studies of the therapy of primary cardiac arrest in our physiologic animal research laboratory.[31,64,77-81] Our findings convinced us by late 2003 that we could not in good faith continue to follow the national and international guidelines for CPR and ECC. We announced our intentions and explained our rationale. Based on CQI, it has been shown in cities, counties, and states where cardiocerebral resuscitation has been instituted that survival from the nation's number of killer has improved. Other methods to improve survival from new approaches to resuscitation have been recently updated by the Utstein Formula for Survival Collaborators and are based on science, education, and local implementation.[82]

Web Sites for CCR and SHARE

www.heart.arizona.edu and azdhs.gov/azshare/

Summary

Out-of-hospital cardiac arrest is major public health problem in the United States, accounting for more premature deaths than any other cause. Guidelines for the therapy of patients with OHCA were little changed from the 1970s to mid-2000, averaging 7.6% for all OHCA and 17.7% for those due to VF. Decades of research lead to the institution of CCR in mid-2000s that resulted in markedly improved survivals of patients with primary OHCAs that averaged 38%. Following the 2005 Guidelines for CPR and EMS, survival of patients with OHCA secondary to VF by some of the best Emergency Medical Systems varied from 7.7% to 39.9%, with a median survival rate of 22%. The only way to know the effectiveness of your Emergency Medical System is to know the survival of patients with OHCA and a shockable rhythm. If it is less than 38%, they should be encouraged to institute CCR and reevaluate the results.

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References

1. Roger V, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2011 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2011;123(4):e18-e209.
2. Roger V, Go AS, Lloyd-Jones DM, et al. Executive summary: heart disease and stroke statistics-2012 update: a report from the American Heart Association. *Circulation*. 2012;125(1):188-197.
3. Lloyd-Jones DM, Berry JD, Ning H, Cai X, Goldberger JJ. Lifetime risk for sudden cardiac death at selected index ages and by risk factor strata and race: cardiovascular lifetime risk pooling project. *Circulation*. 2009;120:S416-S417.
4. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics—2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117(4):e25-e146.
5. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121(4):586-613.
6. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009;119(3):e21-e181.
7. Spaulding SM, Joly LM, Rosenberg A, et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med*. 1997;336(23):1629-1633.
8. Anyfantakis ZA, Baron G, Aubry P, et al. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. *Am Heart J*. 2009;157(2):312-318.
9. Sasson C, Rogers MA, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes*. 2010;3(1):63-81.
10. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation*. 2004;110(21):3385-3397.
11. Cummins RO, Chamberlain D, Hazinski MF, et al. Recommended guidelines for reviewing, reporting, and conducting research on in-hospital resuscitation: the in-hospital 'Utstein style'. A statement for healthcare professionals from the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, the Australian Resuscitation Council, and the Resuscitation Councils of Southern Africa. *Resuscitation*. 1997;34(2):151-183.
12. Bobrow BJ, Spaite DW, Berg RA, et al. Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. *JAMA*. 2010;304(13):1447-1454.
13. Rea TD, Eisenberg MS, Sinibaldi G, White RD. Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. *Resuscitation*. 2004;63(1):17-24.
14. Nichol G, Thomas E, Callaway CW, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA*. 2008;300(12):1423-1431.
15. Cobb LA, Weaver WD, Hallstrom AP, Copass MK. Cardiac resuscitation in the community. The Seattle experience. *Cardiologia*. 1990;35(suppl 1):85-90.
16. Berdowski J, Berg RA, Tijssen JG, Kloster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: systematic review of 67 prospective studies. *Resuscitation*. 2010;81(11):1479-1487.
17. Berg RA, Hilwig RW, Kern KB, Ewy GA. "Bystander" chest compressions and assisted ventilation independently improve outcome from piglet asphyxial pulseless "cardiac arrest". *Circulation*. 2000;101(14):1743-1748.
18. Ewy GA. Cardiocerebral resuscitation: the new cardiopulmonary resuscitation. *Circulation*. 2005;111(16):2134-2142.
19. Kern KB, Valenzuela TD, Clark LL, et al. An alternative approach to advancing resuscitation science. *Resuscitation*. 2005;64(3):261-268.
20. Bobrow BJ, Kern KB. Regionalization of postcardiac arrest care. *Current Opin Crit Care*. 2009;15(3):221-227.
21. Ewy GA, Sanders AB. Alternative approach to improving survival of patients with out-of-hospital primary cardiac arrest. *J Am Coll Cardiol*. 2013;61(2):113-118.
22. Clark JJ, Larsen MP, Culley LL, Graves JR, Eisenberg MS. Incidence of agonal respirations in sudden cardiac arrest. *Ann Emerg Med*. 1992;21(12):1464-1467.
23. Zuercher M, Ewy GA. Gasping during cardiac arrest. *Curr Opin Crit Care*. 2009;15(3):185-188.
24. Zuercher M, Ewy GA, Hilwig RW, et al. Continued breathing followed by gasping or apnea in a swine model of ventricular fibrillation cardiac arrest. *BMC Cardiovasc Disord*. 2010;10:36.
25. Zuercher M, Ewy GA, Otto CW, et al. Gasping in response to basic resuscitation efforts: observation in a Swine model of cardiac arrest. *Crit Care Res Pract*. 2010;1:1-7.
26. Ornato J, Hallagan L, McMahan S, Peeples E, Rostafinski A. Attitudes of BCLS instructors about mouth-to-mouth resuscitation during the AIDS epidemic. *Ann Emerg Med*. 1990;19(2):151-156.
27. Brenner BE, Kauffman J. Reluctance of internist and medical nurses to perform mouth-to-mouth resuscitation. *Arch Intern Med*. 1993;153(15):1763-1769.
28. Brenner B, Stark B, Kauffman J. The reluctance of house staff to perform mouth-to-mouth resuscitation in the inpatient setting: what are the considerations? *Resuscitation*. 1994;28(3):185-193.
29. Brenner B, Kauffman J, Sachter J. Comparison of the reluctance of house staff of metropolitan and suburban hospitals to perform mouth-to-mouth resuscitation. *Resuscitation*. 1996;32(1):5-12.
30. Assar D, Chamberlain D, Colquhoun M, et al. Randomized controlled trials of staged teaching for basic life support. 1. Skill acquisition at bronze stage. *Resuscitation*. 2000;45(1):7-15.

31. Kern KB, Hilwig RW, Berg RA, Sanders AB, Ewy GA. Importance of continuous chest compressions during cardiopulmonary resuscitation: improved outcome during a simulated single lay-rescuer scenario. *Circulation*. 2002;105(5):645-649.
32. Berg RA, Sanders AB, Kern KB, et al. Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. *Circulation*. 2001;104(20):2465-2470.
33. Sayre MR, Berg RA, Cave DM, Page RL, Potts J, White RD. Hands-only (compression-only) cardiopulmonary resuscitation: a call to action for bystander response to adults who experience out-of-hospital sudden cardiac arrest: a science advisory for the public from the American Heart Association Emergency Cardiovascular Care Committee. *Circulation*. 2008;117(16):2162-2167.
34. Iwami T, Kitamura T, Kawamura T, et al. Chest compression-only cardiopulmonary resuscitation for out-of-hospital cardiac arrest with public-access defibrillation: a nationwide cohort study. *Circulation*. 2012;126(24):2844-2851.
35. Panchal AR, Bobrow BJ, Spaite DW, et al. Chest compression-only cardiopulmonary resuscitation performed by lay rescuers for adult out-of-hospital cardiac arrest due to non-cardiac aetiologies. *Resuscitation*. 2013;84(4):435-439.
36. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2005;112(suppl 24):IV1-203.
37. International Liaison Committee on Resuscitation. 2010 International Consensus on Cardiopulmonary Resuscitation and Emergencfy Cardiovascular Care Science with Treatment Recommendations. *Circulation*. 2010;122:S250-S275.
38. Nagao K, Nonogi H, Yonemoto N, et al. Chest compression only bystander cardiopulmonary resuscitation in the 30:2 compression to ventilation ratio era. Nationwide Observational Study. *Circ J*. 2013;77(11):2742-2750.
39. Kellum MJ, Kennedy KW, Ewy GA. Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. *Am J Med*. 2006;119(4):335-340.
40. Kellum MJ, Kennedy KW, Barney R, et al. Cardiocerebral resuscitation improves neurologically intact survival of patients with out-of-hospital cardiac arrest. *Ann Emerg Med*. 2008;52(3):244-252.
41. Berg RA, Kern KB, Sanders AB, Otto CW, Hilwig RW, Ewy GA. Bystander cardiopulmonary resuscitation. Is ventilation necessary? *Circulation*. 1993;88(4 pt 1):1907-1915.
42. Sanders AB, Kern KB, Berg RA, Hilwig RW, Heidenrich J, Ewy GA. Survival and neurologic outcome after cardiopulmonary resuscitation with four different chest compression-ventilation ratios. *Ann Emerg Med*. 2002;40(6):553-562.
43. Steen S, Liao Q, Pierre L, Paskevicius A, Sjoberg T. The critical importance of minimal delay between chest compressions and subsequent defibrillation: a haemodynamic explanation. *Resuscitation*. 2003;58(3):249-258.
44. Guyton AC, Polizio D, Armstrong GG. Mean circulatory filling pressure measured immediately after cessation of heart pumping. *Am J Physiol*. 1954;179(2):261-267.
45. Sorrell VL, Altbach MI, Kern KB, et al. Images in cardiovascular medicine. Continuous cardiac magnetic resonance imaging during untreated ventricular fibrillation. *Circulation*. 2005;111(19):e294.
46. Sorrell VL, Bhatt RD, Berg RA, et al. Cardiac magnetic resonance imaging investigation of sustained ventricular fibrillation in a swine model—with a focus on the electrical phase. *Resuscitation*. 2007;73(2):279-286.
47. Berg RA, Hilwig RW, Kern KB, Ewy GA. Precountershock cardiopulmonary resuscitation improves ventricular fibrillation median frequency and myocardial readiness for successful defibrillation from prolonged ventricular fibrillation: a randomized, controlled swine study. *Ann Emerg Med*. 2002;40(6):563-570.
48. Cobb LA, Fahrenbruch CE, Walsh TR, et al. Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA*. 1999;281(13):1182-1188.
49. Wik L, Hansen TB, Fylling F, et al. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. *JAMA*. 2003;289(11):1389-1395.
50. Bradley SM, Gabriel EE, Aufderheide TP, et al. Survival Increases with CPR by Emergency Medical Services before defibrillation of out-of-hospital ventricular fibrillation or ventricular tachycardia: observations from the Resuscitation Outcomes Consortium. *Resuscitation*. 2009;81(2):155-162.
51. Stiell IG, Nichol G, Leroux BG, et al. Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest. *N Engl J Med*. 2011;365(9):787-797.
52. Yu T, Weil MH, Tang W, et al. Adverse outcomes of interrupted precordial compression during automated defibrillation. *Circulation*. 2002;106(3):368-372.
53. Ewy GA. Defining electromechanical dissociation. *Ann Emerg Med*. 1984;13(9 pt 2):830-832.
54. Wang HE, Simeone SJ, Weaver MD, Callaway CW. Interruptions in cardiopulmonary resuscitation from paramedic endotracheal intubation. *Ann Emerg Med*. 2009;54(5):645-652.
55. Rea T. Protocol or performance. *J Am Coll Cardiol*. 2013;61(2):119-120.
56. Aufderheide TP, Lurie KG. Death by hyperventilation: a common and life-threatening problem during cardiopulmonary resuscitation. *Crit Care Med*. 2004;32(suppl 9):S345-S351.
57. Aufderheide TP, Sigurdsson G, Pirrallo RG, et al. Hyperventilation-induced hypotension during cardiopulmonary resuscitation. *Circulation*. 2004;109(16):1960-1965.
58. Aufderheide TP. The problem with and benefit of ventilations: should our approach be the same in cardiac and respiratory arrest? *Curr Opin Crit Care*. 2006;12(3):207-212.
59. Bobrow BJ, Ewy GA, Clark L, et al. Passive oxygen insufflation is superior to bag-valve-mask ventilation for witnessed ventricular fibrillation out-of-hospital cardiac arrest. *Ann Emerg Med*. 2009;54(5):656-662.
60. Hasegawa K, Hiraide A, Chang Y, Brown D. Association of prehospital advanced airway management with neurologic outcome and survival in patients with out-of-hospital cardiac arrest. *JAMA*. 2013;309(3):257-266.
61. Berg RA, Bobrow BJ. Is an advanced airway harmful during out-of-hospital CPR? *Nat Rev Cardiol*. 2013;10(4):188-189.

62. Hanif MA, Kaji AH, Niemann JT. Advanced airway management does not improve outcome of out-of-hospital cardiac arrest. *Acad Emerg Med*. 2010;17(9):926-931.
63. Egly J, Custodio D, Bishop N, et al. Assessing the impact of prehospital intubation on survival in out-of-hospital cardiac arrest. *Prehosp Emerg Care*. 2011;15(1):44-49.
64. Otto CW, Yakaitis RW, Ewy GA. Effect of epinephrine on defibrillation in ischemic ventricular fibrillation. *Am J Emerg Med*. 1985;3(4):285-291.
65. Zuercher M, Kern KB, Indik JH, et al. Epinephrine improves 24-hour survival in a swine model of prolonged ventricular fibrillation demonstrating that early intraosseous is superior to delayed intravenous administration. *Anesth Analg*. 2011;112(4):884-890.
66. Jacobs IG, Finn JC, Jelinek GA, Oxer HF, Thompson PL. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. *Resuscitation*. 2011;82(9):1138-1143.
67. Youngquist ST, Niemann JT. Regarding "Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial". *Resuscitation*. 2012;83(4): e105-e107.
68. Hayashi Y, Iwami T, Kitamura T, et al. Impact of early intravenous epinephrine administration on coutcomes following out-of-hospital cardiac arrest. *Cir J*. 2012;76(7):1639-1645.
69. Olasveengen TM, Sunde K, Brunborg C, Thowsen J, Steen PA, Wik L. Intravenous drug administration during out-of-hospital cardiac arrest: a randomized trial. *JAMA*. 2009;302(20):2222-2229.
70. Salmen M, Ewy GA, Sasson C. Use of cardiocerebral resuscitation or AHA/ERC 2005 Guidelines is associated with improved survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. *BMJ Open*. 2012;2(5): e0001273. doi:0001210.0001136.
71. Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*. 2007;73(1):29-39.
72. Stiell IG, Wells GA, Field B, et al. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351(7): 647-656.
73. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med*. 2002;346(8):549-556.
74. Spaite DW, Bobrow BJ, Vadeboncoeur TF, et al. The impact of prehospital transport interval on survival in out-of-hospital cardiac arrest: implications for regionalization of post-resuscitation care. *Resuscitation*. 2008;79(1):61-66.
75. Bernard S, Buist M, Monteiro O, Smith K. Induced hypothermia using large volume, ice-cold intravenous fluid in comatose survivors of out-of-hospital cardiac arrest: a preliminary report. *Resuscitation*. 2003;56(1):9-13.
76. Nielsen N, Wetterslv J, Crongerg T, et al. Targeted temperature management at 33 vs 36 degrees centegrate after cardiac arrest. *N Engl J Med*. 2013;369(23):1-10.
77. Ewy GA. Cardiac arrest and resuscitation: defibrillators and defibrillation. *Curr Probl Cardiol*. 1978;2(11):1-71.
78. Ewy GA, Ewy MD, Nuttall AJ, Nuttall AW. Canine transthoracic resistance. *J Appl Physiol*. 1972;32(1):91-94.
79. Sanders A, Kern K, Atlas M, Bragg S, Ewy G. Importance of the duration of inadequate coronary perfusion pressure on resuscitation from cardiac arrest. *J Am Coll Cardiol*. 1985; 6(1):113-118.
80. Kern KB, Ewy GA, Sanders AB, Voorhees WD, Babbs CF, Tacker WA. Neurologic outcome following successful cardiopulmonary resuscitation in dogs. *Resuscitation*. 1986;14(3): 149-155.
81. Kern KB, Sanders AB, Raife J, Milander MM, Otto CW, Ewy GA. A study of chest compression rates during cardiopulmonary resuscitation in humans. The importance of rate-directed chest compressions. *Arch Intern Med*. 1992;152(1):145-149.
82. Soreide E, Morrison L, Hillman K, et al. The formula for survival in resuscitation. *Resuscitation*. 2013;84(11):1487-1493.