

REVIEW ARTICLE

Improving Community Survival Rates from Out-of-Hospital Cardiac Arrest

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Abstract: Out of hospital cardiac arrest affects 350,000 Americans yearly and is associated with a high mortality rate. Improving survival rates in this population rests on the prompt and effective implementation of four key principles. These include 1) early recognition of cardiac arrest 2) early use of chest compressions 3) early defibrillation, which in turn emphasizes the importance of public access defibrillation programs and potential for drone technology to allow for early defibrillation in private or rural settings 4) early and aggressive post-arrest care including the consideration of therapeutic hypothermia, early coronary angiography +/- percutaneous coronary intervention and a hyper-invasive approach to out-of-hospital refractory cardiac arrest.

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1. INTRODUCTION

Out-of-Hospital Cardiac Arrest affects 350,000 Americans each year. Unfortunately, the national survival rate from such an event remains no better than 12% [1], though some communities do better and some worse [2]. The “Chain of Survival” concept has been accepted for decades and remains the roadmap for many communities in their efforts to improve their local survival rates from sudden cardiac death (SCD). The key for this chain to be successful is the EARLY application of each link in the sequence of treating cardiac arrest. The four most important links are;

- Early Recognition of Cardiac Arrest
- Early Use of Chest Compressions to perfuse vital organs
- Early Defibrillation of Shockable Rhythms
- Early and Aggressive Post Arrest Care

2. EARLY RECOGNITION OF CARDIAC ARREST

Though the ultimate goal is to recognize all sudden cardiac arrest in every community, an initiative must be taken with teaching the importance of equating adult witnessed collapse as a sign of cardiac arrest. For quite a long time, the emphasis has been never to perform chest compressions on someone with a beating heart, when in truth, the more serious mistake is to withhold life saving compressions from

someone in cardiac arrest. This shift in thinking is an important step for both professionals and laypersons in community efforts to improve survival rates from sudden cardiac arrest. If an adult suddenly collapses, is unresponsive and not breathing normally, the correct approach is to assume they are in cardiac arrest and begin chest compressions. Data shows that in the rare incidence where non-cardiac arrest patients receive transient chest compressions, the adverse effects are relatively small and manageable [3].

Unresponsiveness is relatively easy for any citizen to determine using the current “shake and shout” approach recommended by the American Heart Association. The key is to recognize what is and what is not “normal breathing” [4]. Normal breathing is a calm process of rhythmic breaths with gentle rise and fall of the thorax, generally at a frequency of 8-16/minute. Victims of sudden cardiac arrest often gasp during the first few minutes of collapse [5, 6]. Gasping or agonal breathing is not “normal breathing” but rather an abrupt, often forceful inspiration and occurs only a few times per minute. Laypersons can mistake this primitive respiratory reflex as “snoring, snorting, moaning, or difficulty in breathing”, and not realize that the patient has suffered a cardiac arrest [7-10].

Emergency medical dispatchers can assist laypersons in recognition of cardiac arrest, on how to access the emergency response system (“911” in the USA). Dispatchers are trained to ask two specific questions in responding to a medical emergency call specifically, “Is the patient conscious?” “Is the patient breathing normally?” [11]. If the caller is uncertain, the dispatcher can listen over the phone themselves to determine normal versus abnormal breathing.

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The European Resuscitation Council (ERC) 2015 guidelines note that if an emergency call describes a person seizing, the dispatcher should have a high index of suspicion for cardiac arrest, since anoxic seizures are common in the early phase of cardiac arrest [12]. The additional advantage of calling “911” early is that once cardiac arrest is diagnosed, the dispatcher can provide the caller with telephone-CPR instructions, typically chest compression-only CPR for adult victims of cardiac arrest.

3. EARLY CHEST COMPRESSIONS

Early initiation of chest compressions in out-of-hospital cardiac arrest (OHCA), by providing a rapid restoration of at least some coronary and cerebral blood flow, is a crucial link in the ‘Chain of Survival’. Central to its implementation is bystander assistance. Bystander cardiopulmonary resuscitation (CPR), prior to the arrival of emergency medical services, improves survival 2-3 fold [13-15]. Observations from over 1000 OHCA in Arizona revealed that bystander CPR was performed in 37% of all arrests [16]. Excluding cardiac arrests that occurred in the presence of an individual with formal CPR training as part of an employment requirement, bystander CPR was performed in only a quarter of cases.

The key to improving survival and neurological outcomes after OHCA lies in increasing rates of bystander CPR. In recent years, several strategies to improve rates of bystander CPR have been implemented worldwide.

4. CHEST COMPRESSION ONLY CPR (CC-ONLY CPR)

CPR with mouth-to-mouth resuscitation raises concern among both the public and healthcare professionals regarding the potential for contracting contagious infectious diseases like HIV [17, 18]. In an attempt to overcome this issue, as well as to simplify basic life support for the general public, we introduced CC-Only CPR in the early 1990s. This was founded on the principle that effective blood flow generation is paramount during cardiac arrest. Prior to its implementation in the community, we showed no difference in hemodynamics, survival or neurological outcomes between CC-only CPR and conventional CPR with ventilation in a series of pre-clinical experiments [19-21]. Following the introduction of CC-Only CPR in the community, we conducted a 5-year prospective observational cohort study of survival in adult OHCA patients and observed an increase in the rates of lay rescuer CPR from 28.2% (95% CI, 24.6%-31.8%) to 39.9% (95% CI, 36.8%-42.9%; $p < 0.001$) [22]. Our findings also revealed improved survival to hospital discharge with CC-Only CPR (13.3% (95% CI, 11.0-15.6%) compared with the conventional CPR (7.8% (95% CI, 5.8%-9.8%) [22].

5. INCREASING ACCESSIBILITY TO BASIC LIFE SUPPORT TRAINING

Certain regions have made a concerted effort at targeting community groups to increase participation in basic life support training. Both Seattle and Amsterdam have implemented a region-wide strategy over the past decades which

led to the vast majority of their public certified in basic life support [23, 24]. Basic life support training not only improves the quality of chest compressions delivered, but provides an opportunity to allay concerns regarding causing greater harm than good by attempting chest compressions.

6. TELEPHONE-CPR

Although the efforts in Amsterdam and Seattle should be commended, increasing accessibility to basic life support certification among the general public remains a challenge due to strategic, organizational and financial constraints. An alternative approach to increase bystander CPR is through Telephone-CPR (T-CPR), comprising bystander CPR directed by instructions from emergency services dispatchers. This is based on the premise that the lay public would be able to recognize cardiac arrest and start resuscitative efforts by following telephone commands from trained dispatch operators. The bystander is asked whether the victim is responsive/conscious and whether he/she is breathing normally. If the bystander responds negatively to both questions, the dispatch operator would recommend initiation of bystander CPR. *Dameff et al.* show that this strategy recognizes the need for T-CPR in 79% of cardiac arrest calls where CPR had not been initiated [25]. However, although recognition for the need of CPR was high and generally took just over 60 seconds (median 69s, IQR 44-104.5), the delivery of bystander T-CPR was only 14% of indicated cases and the median time interval between receipt of call to EMS and T-CPR was 251s (IQR 189-306). The authors cited language, cultural and physical challenges as barriers to performing T-CPR.

CC-Only T-CPR versus conventional T-CPR with rescue breaths has also been debated. The simplicity of CC-Only CPR appears a more attractive option for ease of implementation by a bystander inexperienced in CPR and in a high-stress situation. Individual studies comparing CC-Only CPR versus conventional CPR instructions with rescue ventilation show a favorable trend towards CC-Only CPR instructions [26-28]. A meta-analysis pooling data from combined studies showed a modest, but significantly improved chance of survival with CC-Only T-CPR (risk ratio 1.22, 95% CI 1.01-1.46) [29]. Accordingly, the American Heart Association has recommended the incorporation of CC-Only CPR for T-CPR in its 2012 Statement on EMS dispatch CPR pre-arrival instructions to improve survival from OHCA [30].

7. EMERGING MOBILE TECHNOLOGIES

Mobile phone positioning systems enable trained individuals in the general public to nearby OHCA to be put on alert. This has been a successful strategy in Stockholm, Sweden, where members of the public trained in basic life support were recruited and registered as volunteer mobile rescuers through large media campaigns. These mobile rescuers were alerted if an OHCA was within 500m of their location. In a 25-week retrospective analysis, mobile rescuers arrived prior to EMS in 56% of all OHCA, and of these, 30% had bystander CPR delivered by the mobile rescuer [31].

Similar mobile technologies have taken advantage of these promising results, such as the PulsePoint[®] application,

which is a free mobile application that connects to 911 communication centers and provides real-time information about emergencies, including cardiac arrests in the community. Users can view the exact location of OHCA in the community and the current response status of dispatched units. Application users who have previously indicated that they are trained in CPR are alerted if there is a nearby OHCA and also directs them to the closest public access Automated External Defibrillator (AED).

8. EARLY DEFIBRILLATION

Following early CPR, early defibrillation is the crucial next link in the Chain of Survival. If cardiac arrest is secondary to ventricular fibrillation, defibrillation is an effective treatment and often leads to several more productive life years [32]. However, delay in defibrillation is strongly associated with poor survival [33]. The advent of AEDs has brought about the potential for non-medical personnel, without a duty to respond, to attempt safe defibrillation.

9. PUBLIC ACCESS DEFIBRILLATION (PAD) PROGRAMS

Although the majority of OHCA occur in private residences, 15-20% exist in public arenas suitable for placement of AEDs [34, 35]. In 2004, a large community-based prospective randomized trial provided seminal evidence for the success of PAD programs in the community. The investigators compared survival outcomes following OHCA in community facilities where lay volunteers were trained in both CPR and AED delivery versus CPR alone. Survival to hospital discharge in facilities where volunteers were trained in CPR and AED delivery was higher compared to units assigned to volunteers trained in CPR alone (RR 2.0 95% CI 1.07-3.77) [36]. This data not only showed the benefit of early defibrillation, but also highlighted the concept that nonmedical members of the public, without a duty to respond, can perform safe and effective defibrillation.

More recently, *Baekgaard et al.* systematically reviewed over 40 observational studies investigating the effect of public access defibrillation (PAD) programs on survival outcomes [37]. The median overall survival to hospital discharge after OHCA treated with PAD was 40% (range 9.1-83.3). Importantly, defibrillation by lay members of the public was associated with higher survival rate (median 53% range 26-72) compared to professional first responders (firefighters/police) dispatched by the Emergency Medical Dispatch Center (median 28.6% range 9-76%).

10. TARGETED PUBLIC LOCATIONS FOR AED INSTALLMENT

Appropriately targeted public locations for AED placement are important to ensure a cost-effective strategy to provide prompt access to an AED when required. Settings where there are numerous people, circulating and congregating make for conceptually ideal locations for AED installment.

In casinos, where security officers are trained in AED use, a rapid defibrillation protocol has resulted in over half of patients with ventricular fibrillation cardiac arrest

surviving to hospital discharge (56/105 patients) and nearly three quarters surviving to hospital discharge if first defibrillation was within three minutes of collapse [38].

Targeted AED programs have also been implemented in three inner-city Chicago airports. Between 1999-2001, after their implementation, defibrillation using the on-site AED was delivered in 18 patients with ventricular fibrillation. On all occasions, travelers or airport employees performed defibrillation prior to the arrival of the EMS. Eleven of 18 survived with a good neurological function to hospital discharge. The defibrillator users in six out of the 11 cases of successful resuscitation had never operated an AED nor were trained in its use (although three were physicians). The benefits of targeted AED programs in airports are highlighted when the impressive survival rates observed in Chicago airports are compared to the 2% survival rate for OHCA secondary to ventricular fibrillation in the rest of Chicago [39].

Other busy transport systems worldwide, including the Japanese railways and most recently, Sao Paulo metro system have implemented targeted AED programs, both of which have saved lives [40, 41]. In Sao Paulo, once the full program was instituted, survival to hospital discharge following OHCA secondary to a ventricular arrhythmia was 43% [41].

Targeted AED programs at training and sporting competitions are advantageous, not only because they attract large numbers of spectators, but also because the relative risk of sudden cardiac death in young competitive athletes is nearly three times that of their age-matched sedentary counterparts [42]. The American Heart Association, American College of Cardiology, and Inter-Association Task Force states that every school and college athletic program should strive to have access to an AED within 5 minutes of collapse [43-45]. Because the average time from collapse to EMS arrival on the scene is usually greater than five minutes [46], on-site AED programs appear the most effective way to ensure early defibrillation in sporting arenas.

Targeted AED programs may be important not only in areas of high human traffic, but also in situations where medical assistance may be several hours away. Long-haul flights are one such example and an estimated 1000 cases of cardiac arrest occur annually in commercial aircraft [47]. Quantas and American Airlines have reported good survival outcomes following targeted AED programs in their commercial aircrafts and terminals [48, 49].

11. DRONE TECHNOLOGY

Although targeted AED programs have improved survival from OHCA in a variety of public settings, most OHCA exist in private residences which have slower emergency response times [50]. Static AEDs placed in the homes of individuals with intermediate risk for unexpected cardiac arrest do not significantly improve survival and are not an effective public health strategy to improve survival from OHCA [51]. In 2016, Google patented drone technology for the delivery of medical supplies including AEDs. This shifted the paradigm regarding targeted AED programs, and allowed for the possibility of early defibrillation in private or rural settings. *Boutillier et al.* applied a mathematical model

to a large area of rural and urban regions surrounding Toronto, Canada to investigate the theoretical benefit of drone-delivered AEDs [52]. They calculated that, relative to historical 911 response times, a drone network would reduce the 90th percentile of the AED arrival time by 6 minutes 43 seconds or 10 minutes 34 seconds in urban and rural settings, respectively. Although systematic data from the real-life implementation of drone-delivered AEDs is required, it is nevertheless an exciting and potentially cost-effective solution to provide early defibrillation in OHCA.

12. EARLY AND AGGRESSIVE POST ARREST CARE

Three post-resuscitation therapeutic modalities hold promise for improving survival rates after out-of-hospital cardiac arrest. First, therapeutic hypothermia; second, early coronary angiography and PCI; and third, is not actually a post resuscitation treatment, but a more aggressive, hyper-invasive approach to refractory cardiac arrest occurring out-of-hospital.

13. THERAPEUTIC HYPOTHERMIA

Randomized, prospective trials found that TH effectively improved survival and neurological function of survivors more than a decade ago [53, 54]. More recent randomized clinical trials have failed to find a difference in outcomes between those cooled at 33°C or 36°C [55] or whether cooling was begun in the out-of-hospital setting or in-hospital [56]. However, these neutral results have been misinterpreted by some as evidence that therapeutic hypothermia is ineffective and need not be done post-arrest [57]. Rather, these later studies while showing that it does not seem to matter whether one manages the patient's temperature to 33 or 36, or whether that active management starts in the field or after arrival at the hospital, continue to show excellent outcomes at either temperature target or either site for initiation of cooling. Fig. (1) highlights the survival rates within these

four randomized clinical trials. The randomized data suggests a significant improvement in survival with active cooling compared to the randomized, non-cooled controls from the 2002 publications.

14. EARLY CORONARY ANGIOGRAPHY AND PERCUTANEOUS CORONARY INTERVENTION

Though no current randomized data exists, presently more than 10,000 post-arrest patients have been included in before and after cohort studies strongly suggesting an association between early coronary angiography and PCI and improved survival [58]. Perhaps, the strongest reason in favour of coronary angiography post-arrest is to find and reperfuse culprit coronary arteries responsible for the cardiac arrest. Reports from registries of post-arrest patients with STEMI have shown that 8 out of 10 have an identifiable culprit coronary and that 90% of such culprits are acutely occluded and require timely reperfusion to save myocardium and presumably lives [59]. Combining these figures suggests that 75% of all post-arrest patients with STEMI evidence on their ECG will have an acutely occluded coronary as the precipitating cause of their cardiac arrest. This high incidence has led to both the AHA/ACC and ESC in their recent STEMI guidelines to strongly recommend the use of early coronary angiography and PCI for these patients (Class 1 recommendation) [60, 61]. Those without ST elevation on their post resuscitated ECG have less identified coronary culprits than those with ST elevation, but the proportion of culprits requiring timely intervention is still impressive. One in three such patients without ST elevation have a culprit found at early angiography and 2/3 of such culprits are acutely occluded [59]. This calculates to 1 in 4 having an acutely occluded coronary that should be rapidly reperfused, even though their surface ECG does not indicate such. Unfortunately, this 25% incidence has not resulted in such a strong recommendation from either the AHA/ACC or ESC

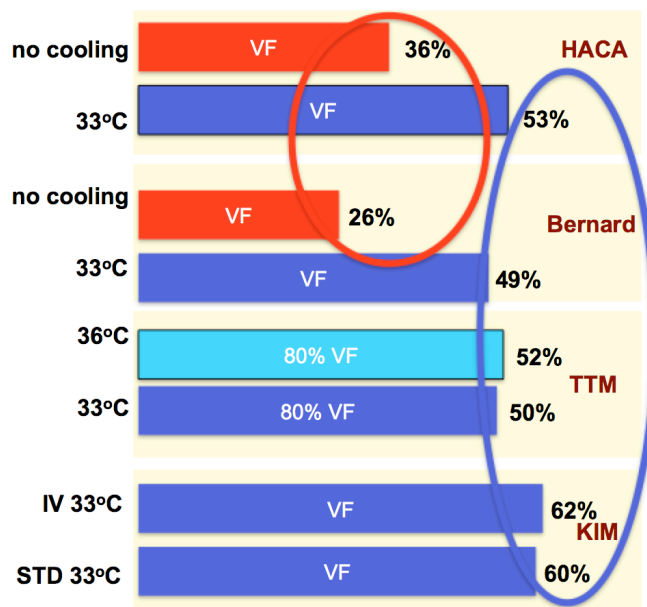


Fig. (1). Consistent improvement in survival to hospital discharge with active cooling post arrest, independent of temperature goal or location where cooling is initiated. Survival with active cooling 54% versus 31% in the non-cooled controls. Survival rates in the 4 RCTs of Therapeutic Hypothermia in Cardiac Arrest.

communities [60, 61]. Still, if myocardium is to be saved, timely reperfusion is crucial, and that is only possible with early coronary angiography leading to early PCI.

15. HYPER-INVASIVE APPROACH TO REFRACTORY OUT-OF-HOSPITAL VFCA

One subgroup of patients suffering from out-of-hospital cardiac arrest that needs additional help is those with ventricular fibrillation that do not respond to standard ACLS efforts. The Seattle Medic 1 program's mantra "no one dies in ventricular fibrillation" highlights this dilemma. Often these are younger patients with an acute catastrophic coronary event leading to cardiac arrest and preventing successful resuscitation, such as an abrupt left main occlusion. A new paradigm of "early transport with on-going CPR", typically mechanical chest compressions, is being espoused as a bridge to more advanced therapies including mechanical circulatory support and high-risk PCI at the hospital. Many details are still being resolved including when to begin transport, *i.e.* when is VF refractory? Several cohort reports have been published showing such a strategy is feasible, and though labor-intensive, can save additional lives [62, 63]. One randomized clinical trial is currently underway in Prague [64].

CONCLUSION

Over the last few decades, communities have experimented with several strategies to improve local survival rates following SCD. First, with regards to early recognition of cardiac arrest, there has been an emphasis on educating the public that withholding life saving compressions is far more serious than performing chest compressions on a beating heart. Second, Chest Compression-only CPR, Telephone-directed CPR and mobile phone positioning systems have enabled the more efficient delivery of effective chest compressions after recognition of OHCA. Third, Public Access Defibrillation programs in the community have allowed greater access to AED, particularly in settings where there is a high volume of human traffic, such as transportation hubs. Further, the advent of drone technology holds real promise for improving the time to defibrillation following OHCA in public, as well as private residences and rural environments. Finally, the addition of an early and aggressive post-arrest care to the traditional Chain of Survival concept may be a critical step in improving rates of survival to hospital discharge after OHCA. While the implementation of all the above strategies requires significant resource allocation, these methods appear to be the key to improving community survival rates from OHCA.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

REFERENCES

- [1] Benjamin EJ, Blaha MJ, Chiuve SE, *et al*, on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2017 update: A report from the American Heart Association. *Circulation* 2017; 135: e146-e603.
- [2] Nichol G, Thomas E, Callaway CW, *et al*. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA* 2008; 300: 1423-31.
- [3] White L, Rogers J, Bloomingdale M, *et al*. Dispatcher-assisted cardiopulmonary resuscitation: Risks for patients not in cardiac arrest. *Circulation* 2010; 121: 91-7.
- [4] Field JM, Hazinski MF, Sayre MR, *et al*. Part 1: Executive summary: 2010 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010; 122(suppl 3): S640-56.
- [5] Clark JJ, Larsen MP, Culley LL, *et al*. Incidence of agonal respirations in sudden cardiac arrest. *Ann Emerg Med* 1992; 21: 1464-7.
- [6] Bobrow BJ, Zuercher M, Ewy GA, *et al*. Gaspings during cardiac arrest in humans is frequent and associated with improved survival. *Circulation* 2008; 118: 2550-4.
- [7] Bang A, Herlitz J, Martinell S. Interaction between emergency medical dispatcher and caller in suspected out-of-hospital cardiac arrests calls with focus on agonal breathing. A review of 100 tape recordings of true cardiac arrest cases. *Resuscitation* 2003; 56: 25-34.
- [8] Breckwoldt J, Schloesser A, Arntz HR. Perceptions of collapse and assessment of cardiac arrest by bystanders of out-of-hospital cardiac arrest (OOHCA). *Resuscitation* 2009; 80: 1108-13.
- [9] Fukushima H, Imanishi M, Iwami T, *et al*. Abnormal breathing of sudden cardiac arrest victims described by laypersons and its association with emergency medical service dispatcher-assisted cardiopulmonary resuscitation instruction. *Emerg Med J* 2015; 32: 314-7.
- [10] Fukushima H, Panczyk M, Hu C, *et al*. Description of abnormal breathing is associated with improved outcomes and delayed telephone cardiopulmonary resuscitation instructions. *J Am Heart Assoc* 2017; 6: e005058.
- [11] Bobrow BJ, Spaite DW, Vadeboncoeur TF, *et al*. Implementation of a regional telephone cardiopulmonary resuscitation program and outcomes after out-of-hospital cardiac arrest. *JAMA Cardiol* 2016; 1(3): 294-302.
- [12] Monsieurs KC, Nolan JP, Bossaert LL, *et al*. European Resuscitation Council guidelines for resuscitation 2015. Section 1. Executive summary. *Resuscitation* 2015; 95: 1-80.
- [13] Wissenberg M, Lippert FK, Folke F, *et al*. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. *JAMA* 2013; 310(13): 1377-84.
- [14] Hollenberg J, Herlitz J, Lindqvist J, *et al*. Improved survival after out-of-hospital cardiac arrest is associated with an increase in proportion of emergency crew-witnessed cases and bystander cardiopulmonary resuscitation. *Circulation* 2008; 118(4): 389-96.
- [15] Abella BS, Aufderheide TP, Eigel B, *et al*. Reducing barriers for implementation of bystander-initiated cardiopulmonary resuscitation: A scientific statement from the American Heart Association for healthcare providers, policymakers, and community leaders regarding the effectiveness of cardiopulmonary resuscitation. *Circulation* 2008; 117(5): 704-9.
- [16] Vadeboncoeur T, Bobrow BJ, Clark L, *et al*. The Save Hearts in Arizona Registry and Education (SHARE) program: Who is performing CPR and where are they doing it? *Resuscitation* 2007; 75(1): 68-75.
- [17] Ornato JP, Hallagan LF, McMahan SB, Peebles EH, Rostafinski AG. Attitudes of BCLS instructors about mouth-to-mouth resuscitation during the AIDS epidemic. *Ann Emerg Med* 1990; 19(2): 151-6.
- [18] Brenner BE, Kauffman J. Reluctance of internists and medical nurses to perform mouth-to-mouth resuscitation. *Arch Intern Med* 1993; 153(15): 1763-9.
- [19] Berg RA, Kern KB, Sanders AB, Otto CW, Hilwig RW, Ewy GA. Bystander cardiopulmonary resuscitation. Is ventilation necessary? *Circulation* 1993; 88(4 Pt 1): 1907-15.
- [20] Berg RA, Wilcoxson D, Hilwig RW, *et al*. The need for ventilator support during bystander CPR. *Ann Emerg Med* 1995; 26(3): 342-50.

- [21] Kern KB, Hilwig RW, Berg RA, Ewy GA. Efficacy of chest compression-only BLS CPR in the presence of an occluded airway. *Resuscitation* 1998; 39(3): 179-88.
- [22] Bobrow BJ, Clark LL, Ewy GA, *et al.* Minimally interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. *JAMA* 2008; 299: 1158-65.
- [23] Rea TD, Helbock M, Perry S, *et al.* Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: survival implications of guideline changes. *Circulation* 2006; 114(25): 2760-5.
- [24] Berdowski J, Blom MT, Bardai A, Tan HL, Tijssen JGP, Koster RW. Impact of onsite or dispatched automated external defibrillator use on survival after out-of-hospital cardiac arrest. *Circulation* 2011; 124(20): 2225-32.
- [25] Dameff C, Vadeboncoeur T, Tully J, *et al.* A standardized template for measuring and reporting telephone pre-arrival cardiopulmonary resuscitation instructions. *Resuscitation* 2014; 85(7): 869-73.
- [26] Hallstrom A, Cobb L, Johnson E, Copass M. Cardiopulmonary resuscitation by chest compression alone or with mouth-to-mouth ventilation. *N Engl J Med* 2000; 342(21): 1546-53.
- [27] Rea TD, Fahrenbruch C, Culley L, *et al.* CPR with chest compression alone or with rescue breathing. *N Engl J Med* 2010; 363(5): 423-33.
- [28] Svensson L, Bohm K, Castren M, *et al.* Compression-only CPR or standard CPR in out-of-hospital cardiac arrest. *N Engl J Med* 2010; 363(5): 434-42.
- [29] Hupfl M, Selig HF, Nagele P. Chest-compression-only versus standard cardiopulmonary resuscitation: a meta-analysis. *Lancet (London, England)* 2010; 376(9752): 1552-7.
- [30] Lerner EB, Rea TD, Bobrow BJ, *et al.* Emergency medical service dispatch cardiopulmonary resuscitation prearrival instructions to improve survival from out-of-hospital cardiac arrest: A scientific statement from the American Heart Association. *Circulation* 2012; 125(4): 648-55.
- [31] Ringh M, Fredman D, Nordberg P, Stark T, Hollenberg J. Mobile phone technology identifies and recruits trained citizens to perform CPR on out-of-hospital cardiac arrest victims prior to ambulance arrival. *Resuscitation* 2011; 82(12): 1514-8.
- [32] Cobb LA, Baum RS, Alvarez H 3rd, Schaffer WA. Resuscitation from out-of-hospital ventricular fibrillation: 4 years follow-up. *Circulation* 1975; 52(6 Suppl): III223-35.
- [33] Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: A logistic regression survival model. *Circulation* 1997; 96(10): 3308-13.
- [34] Becker L, Eisenberg M, Fahrenbruch C, Cobb L. Public locations of cardiac arrest. Implications for public access defibrillation. *Circulation* 1998; 97(21): 2106-9.
- [35] Pell JP, Sirel JM, Marsden AK, Ford I, Walker NL, Cobbe SM. Potential impact of public access defibrillators on survival after out of hospital cardiopulmonary arrest: Retrospective cohort study. *BMJ* 2002; 325(7363): 515.
- [36] The public access defibrillation trial investigators. Public access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004; 351: 637-46.
- [37] Baekgaard J, Viereck S, Moller T, Ersboll A, Lippert F, Folke F. The effects of public access defibrillation on survival after out-of-hospital cardiac arrest: A systematic review of observational studies. *Circulation* 2017; 136(10): 954-65.
- [38] Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *N Engl J Med* 2000; 343(17): 1206-9.
- [39] Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. *N Engl J Med* 2002; 347(16): 1242-7.
- [40] Murakami Y, Iwami T, Kitamura T, *et al.* Outcomes of out-of-hospital cardiac arrest by public location in the public-access defibrillation era. *J Am Heart Assoc* 2014; 3(2): e000533.
- [41] Gianotto-Oliveira R, Gonzalez MM, Vianna CB, *et al.* Survival after ventricular fibrillation cardiac arrest in the Sao Paulo metropolitan subway system: First successful targeted Automated External Defibrillator (AED) program in Latin America. *J Am Heart Assoc* 2015; 4(10): e002185.
- [42] Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003; 42(11): 1959-63.
- [43] Hazinski MF, Markenson D, Neish S, *et al.* Response to cardiac arrest and selected life-threatening medical emergencies: The medical emergency response plan for schools—a statement for healthcare providers, policymakers, school administrators, and community leaders. *Ann Emerg Med* 2004; 43(1): 83-99.
- [44] Myerburg RJ, Estes NAM 3rd, Fontaine JM, Link MS, Zipes DP. Task Force 10: automated external defibrillators. *J Am Coll Cardiol* 2005; 45(8): 1369-71.
- [45] Drezner JA, Courson RW, Roberts WO, Mosesso VNJ, Link MS, Maron BJ. Inter-association task force recommendations on emergency preparedness and management of sudden cardiac arrest in high school and college athletic programs: A consensus statement. *Clin J Sport Med Off J Can Acad Sport Med* 2007; 17(2): 87-103.
- [46] Nichol G, Stiell IG, Laupacis A, Pham B, Maio VJ De, Wells GA. A cumulative meta-analysis of the effectiveness of defibrillator capable emergency medical services for victims of out-of-hospital cardiac arrest. *Ann Emerg Med* 1999; 34(4 Pt 1): 517-25.
- [47] Crewdson J. Code blue: Survival in the sky. *Chicago Tribune* 1996.
- [48] O'Rourke MF, Donaldson E, Geddes JS. An airline cardiac arrest program. *Circulation* 1997; 96(9): 2849-53.
- [49] Page RL, Joglar JA, Kowal RC, *et al.* Use of automated external defibrillators by a U.S. airline. *N Engl J Med* 2000; 343(17): 1210-6.
- [50] Swor RA, Jackson RE, Compton S, *et al.* Cardiac arrest in private locations: Different strategies are needed to improve outcome. *Resuscitation* 2003; 58(2): 171-6.
- [51] Bardy GH, Lee KL, Mark DB, *et al.* Home use of automated external defibrillators for sudden cardiac arrest. *N Engl J Med* 2008; 358(17): 1793-804.
- [52] Boutillier JJ, Brooks SC, Janmohamed A, *et al.* Optimizing a drone network to deliver automated external defibrillators. *Circulation* 2017; 135(25): 2454-65.
- [53] Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med* 2002; 346: 549-56.
- [54] Bernard SA, Gray TW, Buist MD *et al.* Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002; 346: 557-63.
- [55] Nielsen N, Wetterslev J, Cronberg T, *et al.* for the TTM Trial Investigators. Targeted temperature management at 33 degrees C versus 36 degrees C after cardiac arrest. *N Engl J Med* 2013; 369: 2197-206.
- [56] Kim F, Nichol G, Maynard C, *et al.* Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest: A randomized clinical trial. *JAMA* 2014; 311(1): 45-52.
- [57] Little NE, Feldman EL. Therapeutic hypothermia after cardiac arrest without return of consciousness: Skating on thin ice. *JAMA Neurol* 2014; 71(7): 823-4.
- [58] Lotun K, Kern KB. How much is enough? *Circ Cardiovasc Interv* 2015; 8: e003075.
- [59] Kern KB, Lotun K, Patel N, *et al.* Outcomes of comatose cardiac arrest survivors with and without ST elevation: The importance of coronary angiographic findings. *J Am Coll Cardiol Interv* 2015; 8: 1031-40.
- [60] O'Gara PT, Kushner FG, Ascheim DD, *et al.* 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013; 61: 485-510.
- [61] Steg PG, James SK, Atar D, *et al.* ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012; 33: 2569-619.
- [62] Stub D, Berbarth S, Pellegrino V, *et al.* Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER Trial). *Resuscitation* 2015; 86: 88-94.
- [63] Yannopoulos D, Bartos JA, Raveebdran G, *et al.* Coronary artery disease in patients with out-of-hospital refractory ventricular fibrillation cardiac arrest. *J Am Coll Cardiol* 2017; 70: 1109-17.
- [64] Belohlavek J, Kucera K, Jarkovsky J, *et al.* Hyperinvasive approach to out-of-hospital cardiac arrest using mechanical chest compression device, prehospital intraarrest cooling, extracorporeal life support and early invasive assessment compared to standard of care. A randomized, parallel groups comparative study proposal. "Prague OHCA Study". *J Translational Med* 2012; 10: 163.