Optimizing Survival from Out-of-Hospital Cardiac Arrest

ERIK P. HESS, M.D. M.Sc.* and ROGER D. WHITE, M.D., F.A.C.C.†

From the *Department of Emergency Medicine, Division of Emergency Medicine Research, Mayo Clinic College of Medicine; and †Department of Anesthesiology and Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic College of Medicine, Medical Director, City of Rochester Early Defibrillation Program, Rochester, Minnesota, USA

Survival From Out-of-Hospital Cardiac Arrest. Cardiac arrest is an important public health problem and often occurs in the out-of-hospital setting in patients without a prior history of heart disease. Very few communities or emergency medical service (EMS) systems report survival rates for out-of-hospital cardiac arrest. Among those who do, survival rates vary substantially between cities, due in large part to community differences in the chain of survival. To improve survival in cardiac arrest, care must be optimized at each point along the cardiac arrest continuum, including a rapid emergency response, provision of cardiopulmonary resuscitation (CPR) by bystanders, delivery of high-quality chest compressions with minimal interruptions by first responders, rapid defibrillation, and optimization of postresuscitation care, including therapeutic hypothermia. Important current initiatives to improve cardiac arrest survival include hands-only CPR delivered by laypersons prior to the arrival of EMS, dispatcher-assisted CPR, and implementation of hospital-based therapeutic hypothermia protocols to improve postresuscitation care. Optimizing cardiac arrest survival requires a team effort between EMS directors, emergency physicians, cardiologists, hospital leadership, and the public. *(J Cardiovasc Electrophysiol, Vol. 21, pp. 590-595, May 2010)*

automated external defibrillator (AED), defibrillation, cardiac arrest, cardiopulmonary resuscitation (CPR), emergency medical services, sudden death

Introduction

Out-of-hospital cardiac arrest (OHCA) is both a major public health problem and an important issue for the clinician. Extrapolation, on a population basis, from U.S. Census Bureau data suggests that a total of 154,800 OHCAs occur annually.[1] Of these, 60% are treated by emergency medical service (EMS) providers, and 50% occur in individuals with no prior history of cardiac disease.[2] Despite significant advances in emergency cardiac care, survival rates from OHCA remain low. Relatively few cities or EMS agencies report survival from OHCA. Among those who do, survival ranges from 7.7% to 39.9%,[3] with only a few cities reporting rates higher than this.[4,5] This large disparity in survival between cities is due in large part to community differences in the chain of survival.[6]

The "chain of survival" concept, as originally proposed by the Advanced Cardiac Life Support (ACLS) Subcommittee and the Emergency Cardiac Care Committee of the American Heart Association (AHA) in 1991,[7] emphasizes 4 key links that must be executed well to optimize survival in OHCA, including early access, early cardiopulmonary resuscitation (CPR), early defibrillation, and early advanced care. In this article, we will discuss the latest advances in cardiac arrest care as they pertain to each link in the chain of survival. We will also offer suggestions for immediate implementation to optimize survival from cardiac arrest in the community.

The First Link—Early Access

When a patient experiences a cardiac arrest outside the hospital, a 911 call must be made as rapidly as possible. This call marks the beginning of the resuscitation chain. Many potential delays can occur after a bystander recognizes a medical emergency. Time spent finding a telephone, speaking to an emergency dispatcher, and the time to route the call to the correct response station or vehicle all pose potential delays to initiation of the emergency response. Time from patient collapse to initiation of the 911 call is difficult to determine, as estimates of the time of collapse obtained from bystanders are often unreliable. As a consequence, time of call receipt is the first reliable time point; it is the recommended measurable anchor point to indicate activation of the EMS system. As soon as a dispatcher contacts an emergency responder, ambulance response time begins. Arrival of the ambulance on scene marks the end of the ambulance response time (Table 1). After arrival of the ambulance on scene, however, additional time may elapse before emergency responders actually arrive at the patient and initiate treatment. It is for this reason that the interval from receipt of the 911 call to

Dr. Hess is supported in part by a grant from the American Heart Association, the Society for Academic Emergency Medicine, and the Emergency Medicine Foundation (Award ID # 0775030N).

No disclosures.

Address for correspondence: Roger D. White, M.D., Department of Anesthesiology and Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905, USA. Fax: 507-255-6463; E-mail: white.roger@mayo.edu

Manuscript received 17 November 2009; Revised manuscript received 25 November 2009; Accepted for publication 1 December 2009.

doi: 10.1111/j.1540-8167.2009.01706.x

TABLE 1

Recommended Critical Time Intervals in the Emergency Medical System Response to Out-of-Hospital Cardiac Arrest

Time Interval	Definition
Response time*	Time from 911 call receipt to arrival of first responders on scene
Call-to-on**	Time from 911 call receipt to powering on of the defibrillator
Call-to-shock	Time from 911 call receipt to the first defibrillation
Call-to-CPR	Time from 911 call receipt to the initiation of CPR

*Response time is a less reliable indicator of EMS performance, as additional time may elapse between arrival on scene and arrival of first responders at the patient's side to initiate treatment.
**In our EMS system, first responders are instructed to power on the defibrillator on arrival to the patient's side.
CPR = cardiopulmonary resuscitation; EMS = emergency medical service.

delivery of EMS care (CPR or defibrillation) should be used as the preferred measure of EMS system performance. Both the time of call receipt and the time of the first shock or initiation of CPR can be reliably captured. In our system, we routinely calculate call-to-shock time and call-to-on time by synchronizing all defibrillators to the Universal Time Coordinate.

In an effort to decrease the interval from call receipt to the initiation of emergency treatment, many EMS systems have invested in more ambulances. This approach is costly and inefficient. An alternative is to utilize existing resources, e.g., by incorporating additional first responders such as police and fire-rescue personnel in the emergency response. In many locations, fire departments play a major or primary role in the EMS system, but that is not commonly the case with police departments. This approach requires close collaboration between leaders of EMS and police and fire departments, but it can provide a rapid emergency response, e.g., provision of rapid defibrillation. In our system, we included police in the emergency response in late 1990 and fire-rescue personnel in 1998.[8] We have observed a progressive increase in survival to hospital discharge as police and then fire personnel were incorporated in the emergency response. This increase in survival can be attributed, in part, to relatively rapid call-to-shock times.[4] At the time of call receipt, Public Safety Communications dispatches both police and fire-rescue personnel to the scene. The call is then transferred directly to a hospital-based Emergency Communications Center, which then dispatches a paramedic-staffed advanced life support (ALS) ambulance nearly simultaneously. The agency that first arrives on scene initiates resuscitation and provides defibrillation when indicated. We refer to the near simultaneous activation of police, fire, and paramedic ALS ambulances as a nontiered emergency response. Structuring the emergency response in this way can limit the length of time that elapses before initiation of life-saving treatment and improve survival from cardiac arrest.

The Second Link—Early CPR

Bystanders should initiate CPR as soon as possible after recognition of cardiac arrest. If a lone rescuer witnesses a cardiac arrest, the rescuer should activate the emergency response system prior to starting CPR. If more than one person is present on scene, however, CPR should be started simultaneous with activation of the emergency response. The Ontario Prehospital Advanced Life Support (OPALS) study, one of the largest prehospital studies on cardiac arrest patients, enrolled 5,335 patients with cardiac arrest of presumed cardiac origin treated by EMS providers. Using multivariable logistic regression, the following variables were found to be independently associated with survival: bystander-witnessed arrest, bystander CPR, CPR by fire or police, and ambulance response time. Of these independent predictors of survival, bystander CPR was the potentially modifiable factor that had the strongest association with survival to hospital discharge (odds ratio 2.98, 95% CI 2.07–4.29).[9] A recent meta-analysis of 79 studies involving 142,740 patients emphasized the association between survival and bystander CPR, ventricular fibrillation (VF) as the initial rhythm, and sustained return of spontaneous circulation on-scene.[10] Despite the known association between bystander CPR and survival, the prevalence of bystander CPR is unacceptably low in most EMS systems, and at 50.4% ours is no exception.[11] One approach to increasing the prevalence of bystander CPR is instruction by dispatchers at the time of receipt of the 911 call. Dispatcher-assisted CPR has been shown to improve survival in cardiac arrest,[12] and many EMS systems have protocols in which dispatchers routinely instruct callers in the provision of CPR prior to the arrival of first responders.

The 2005 AHA guidelines for CPR and Emergency Cardiovascular Care also emphasized the need to increase the quality of CPR delivered to cardiac arrest victims.[13] Whereas the 2000 guidelines recommended a 15:2 compression to ventilation ratio, the 2005 guidelines increased the ratio to 30:2 to minimize the frequency of interruptions and maximize coronary and cerebral perfusion during cardiac arrest. This recommendation was based on evidence from animal studies that inadequate blood flow secondary to frequent interruptions in chest compressions or inadequate depth and rate of compressions during cardiac arrest adversely effects both restoration of spontaneous circulation and neurologic outcome.[14] Clinical studies of CPR in both the in-hospital and out-of-hospital settings have documented deficiencies in the quality of CPR delivered by healthcare professionals.[15,16] A recent multicenter prospective observational study including patients from 11 sites across the U.S. and Canada demonstrated that increasing the proportion of time in which chest compressions were performed during each minute of CPR (chest compression fraction) was independently predictive of improved survival to hospital discharge in VF OHCA.[17] The 2005 guidelines define high-quality chest compressions as compressions of adequate rate (100 compressions per minute) and depth (1–1.5 inches), with full chest recoil between compressions and minimal interruptions.

The AHA Emergency Cardiovascular Care committee recently published an update of the 2005 guidelines summarizing the research published since 2005 on hands-only (compression only) CPR.[18] Since 2005 several nonrandomized observational human studies have been published comparing conventional (30 compressions to 2 ventilations) to hands-only CPR.[19–22] Although these studies could not assess or control for the quality of bystander CPR, none of them demonstrated an adverse impact on survival when ventilations were omitted from the bystander CPR sequence. Given these data, the relatively low prevalence of bystander CPR, and the potential for increasing the provision of bystander

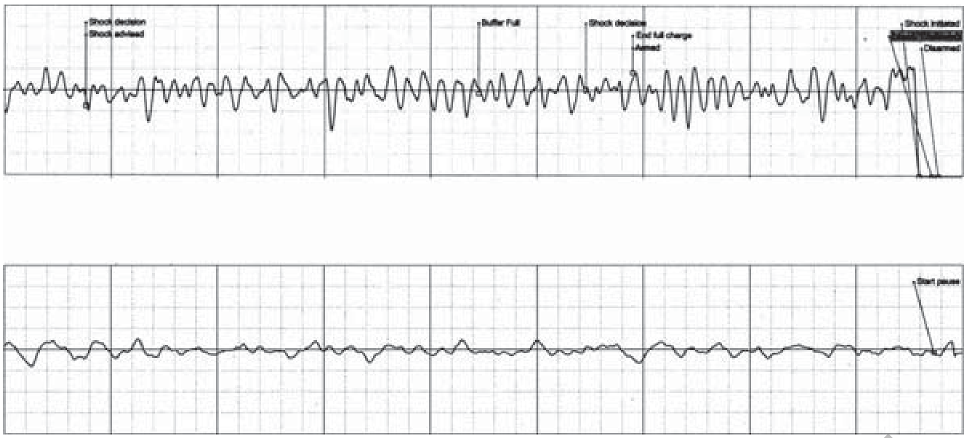

Figure 1. *Automated external defibrillator algorithm decision: Shock first or cardiopulmonary resuscitation (CPR) first. The upper panel represents shockable ventricular fibrillation (VF) because of the amplitude, frequency, and conduction characteristics. In the lower panel, the VF demonstrates characteristics that are likely to improve with a period of CPR before attempting defibrillation. These morphologic differences in the VF waveform are commonly observed with shorter and longer response times, respectively.*

CPR by simplifying the resuscitation sequence, the committee recommended that bystanders use either chest compression only or conventional CPR to achieve the goal of providing effective chest compressions to victims of witnessed OHCA.[18]

The Third Link—Early Defibrillation

Early defibrillation is a critical component of the chain of survival because the likelihood of successful defibrillation decreases rapidly over time. Physiologically, cardiac stores of myocardial oxygen and metabolic substrates are depleted as time passes in VF, thus decreasing the effectiveness of delivered shocks. Provision of an initial period of CPR prior to defibrillation has been proposed as a mechanism to “prime” the heart by supplying much needed oxygen and substrates, thus increasing shock effectiveness. Preliminary analysis of ECG waveform characteristics during OHCA suggests that the morphology of the VF waveform may evolve as time passes in VF.[23] Figure 1 shows high amplitude, course VF (likely to be encountered early after cardiac arrest) in which immediate defibrillation may be the most effective therapy (panel A) and lower amplitude, fine VF that may benefit from a period of CPR before defibrillation (panel B).

Given this interaction between VF, CPR, and shock effectiveness, the two primary questions addressed in the 2005 AHA guidelines related to whether victims of OHCA should receive CPR or shocks as initial treatment and the number of shocks that should be delivered in sequence before resumption of CPR. Given the changes in myocardial physiology that occur as time passes in VF, Weisfeldt and Becker proposed a 3-phase time sensitive model for cardiac arrest.[24] According to this model, defibrillation is the most effective initial treatment for patients encountered in the first or electrical phase (extending from onset of cardiac arrest to approximately 4 minutes following arrest). In the second or circulatory phase of cardiac arrest (extending from 4 to 10 minutes from the arrest), an initial period of CPR should be provided before defibrillation to increase the likelihood of shock effectiveness. After approximately 10 minutes of cardiac arrest (the metabolic phase), the effectiveness of both CPR and defibrillation is limited. During this phase, therapies directed at modulation of oxidant damage, immune system mediators, apoptosis, and microvascular injury are most likely to be effective. Results of both a nonrandomized observational study[25] and a randomized controlled trial[26] support the accuracy of the time sensitive model of cardiac arrest. When the EMS response interval was greater than 4–5 minutes, an initial period of CPR resulted in higher rates of defibrillation, return of spontaneous circulation, and survival compared with those outcomes in OHCA victims who received defibrillation as the initial treatment. For this reason, the 2005 guidelines recommend five cycles of CPR (30:2 compression to ventilation ratio; approximately $1\frac{1}{2}$ to 3 minutes) be provided prior to rhythm analysis and defibrillation when response times exceed approximately 5 minutes.[27] When the call-to-response interval is $<$ 4 to 5 minutes and the arrest is witnessed, defibrillation should be the initial treatment.[4] However, this remains an area of ongoing controversy and it will be re-addressed during development of the 2010 guidelines. Two more recent studies did not confirm the benefit of provision of CPR for periods of 90 seconds or 3 minutes before shock delivery.[28,29]

At the time of the 2005 guidelines, there were no studies that directly compared 1-shock versus 3-shock protocols for VF arrest. Since the publication of the guidelines an animal study reported increased survival and decreased interruptions in CPR in those resuscitated with a 1-shock compared to a 3-shock protocol.[30] Recent human studies also support the deleterious effects of interruptions in CPR. Eftestol *et al.* observed a decreased probability of shock success with increasing interruptions in CPR,[31] and a recent multicenter observational study demonstrated increasing survival as the proportion of time in which chest compressions were delivered in each minute of CPR increased.[17] For these reasons, it is recommended that the rescuer deliver 1 shock and immediately resume CPR for VF/VT in the pulseless arrest algorithm. This approach minimizes “hands-off” time during the resuscitation and increase the likelihood of shock success should additional shocks be required.

Evidence from both in-hospital and out-of-hospital studies has demonstrated increased effectiveness of biphasic waveform shocks compared with monophasic waveforms for defibrillation of VF. Studies comparing fixed versus escalating energy levels for initial and subsequent shocks, however, have reported mixed results. The BIPHASIC trial, a prehospital clinical trial comparing fixed versus escalating energy levels in OHCA, observed higher rates of VF termination for both initial and subsequent shocks in patients randomized to an escalating energy protocol.[32] Whether the differences observed in this trial were due to proprietary differences in biphasic waveform design between defibrillator manufacturers or to a true difference in effectiveness between a nonescalating and escalating energy protocol is not certain. In our setting, we employ a nonescalating energy protocol for all defibrillation shocks delivered by police and fire-rescue personnel. Analysis of the effectiveness of biphasic shocks in our setting revealed a high degree of shock success with the initial shock (>90%), and we observed no significant difference in shock effectiveness between initial and subsequent shocks.[33] Additional studies are needed to determine the most effective biphasic waveform for defibrillation, optimal energy levels, and whether to use escalating or nonescalating energy protocols for any given waveform design.

The Fourth Link—Early Advanced Care

ALS interventions such as endotracheal intubation and administration of cardiac medications have long been thought to improve outcome in cardiac arrest. The 2000 guidelines recommended vasopressin as an alternative to epinephrine in cardiac arrest largely in response to both animal studies and data from a small clinical trial of 40 VF OHCA victims that reported increased 24-hour survival in patients randomized to receive vasopressin.[34] Findings from a subsequent meta-analysis of 1,519 patients from 5 randomized trials, however, indicated no survival advantage of vasopressin over epinephrine.[35] Although the landmark clinical trial on amiodarone in VF OHCA victims demonstrated increased survival to hospital admission,[36] increased survival to hospital discharge in the amiodarone group was not observed, and no subsequent studies have demonstrated increased survival to hospital discharge related to amiodarone administration. A recent clinical trial in Oslo, Norway randomized 851 OHCA victims to receive either ACLS with intravenous drug administration or ACLS without access to intravenous drugs.[37] Compared with the group without access to intravenous drugs, the group with access to IV drugs had a higher rate of return of spontaneous circulation and survival to hospital admission but no difference in survival to hospital discharge or survival with favorable neurological outcome. Results from the OPALS study also confirmed the relative ineffectiveness of ALS interventions in cardiac arrest; no improvement in survival was observed with the addition of ALS-trained EMS providers in systems previously optimized to provide rapid defibrillation.[38] Although paramedics continue to provide ALS care to OHCA victims, recent efforts to improve survival after cardiac arrest have been directed toward improving postresuscitation care.

Compared with the focal tissue ischemia that occurs with myocardial infarction, establishment of reperfusion after cardiac arrest is not a definitive treatment. Out of every 100 cardiac arrest victims, return of spontaneous circulation may be achieved in approximately 30, but, on average, only 5 survive to hospital discharge.[39] Consequently, efforts to improve postresuscitation care have potential to lead to substantial improvements in cardiac arrest survival. A recent Cochrane meta-analysis of randomized trials comparing normothermia to mild induced hypothermia (therapeutic cooling to 32°C to 34°C) in comatose survivors of VF OHCA reported improved survival and neurologic outcome in patients treated with therapeutic hypothermia compared with normothermia.[40] One of the new recommendations in the 2005 guidelines was the provision of therapeutic hypothermia to survivors of VF OHCA who are unresponsive on arrival to the hospital. Despite this recommendation, many hospitals have not successfully implemented a therapeutic hypothermia protocol.[41] Implementation of a therapeutic hypothermia protocol is a multidisciplinary effort that requires substantial personnel and hospital resources, and this is one reason many hospitals have not developed a therapeutic hypothermia protocol. This disparity in postresuscitation care has led to the concept of "cardiac arrest centers" that provide high-quality postresuscitation care, including therapeutic hypothermia, for cardiac arrest victims. Preliminary research suggests that longer out-of-hospital transport intervals are not associated with decreased survival in cardiac arrest,[42] further supporting the safety of transporting cardiac arrest patients to specialized cardiac arrest centers. Clinical trials to assess the efficacy and safety of bypassing local hospitals to take patients to regional cardiac arrest centers are in the planning phases.

Recommendations to Improve Cardiac Arrest Survival in the Community

We have several recommendations for implementation to optimize cardiac arrest survival in your community.

1. *Develop a community cardiac arrest registry*. Relatively few EMS systems document and report cardiac arrest survival. Establishing the infrastructure needed to collect critical data elements and determining the baseline survival rate is the first step toward improving cardiac arrest survival.
2. *Establish a rapid dispatch for cardiac arrest*. When a caller reports observations potentially compatible with cardiac arrest, EMS units should be immediately dispatched. Additional information obtained by the dispatcher can be relayed to emergency response units while en route to the scene.
3. *Develop a protocol for dispatcher-assisted CPR*. This can increase the prevalence and quality of bystander CPR, which in turn optimizes the efficacy of defibrillation.
4. *Establish a reliable method to measure the interval from the time of receipt of the 911 call to initiation of CPR or defibrillation*. As pointed out earlier, in our system all defibrillators are synchronized to the Universal Time Coordinate on a daily basis, or immediately following download of data from first responder automated external defibrillators (AEDs). Rapid response times are critical to cardiac arrest survival, and precise measurement of critical time intervals is necessary to objectively monitor system performance.
5. *Promote early defibrillation*. Incorporating AED-equipped police and fire-rescue personnel into the EMS response is an untapped resource in many EMS systems and has potential to substantially decrease response time. As patients who experience a cardiac arrest in a public location are more likely to be witnessed, to receive

bystander CPR, and to have VF as the initial rhythm, community initiatives to improve public access to defibrillation also have potential to improve survival for arrests that occur in public locations.

Conclusions

Cardiac arrest is an important public health problem and often occurs in the out-of-hospital setting in patients without a prior history of heart disease. Very few communities or EMS systems report survival rates for OHCA. Among those who do, survival rates vary substantially among cities, due in large part to community differences in the chain of survival. To improve survival in cardiac arrest, care must be optimized at each point along the cardiac arrest continuum, including a rapid emergency response, provision of CPR by bystanders, delivery of high-quality chest compressions with minimal interruptions by first responders and all others providing CPR, rapid defibrillation, and optimization of postresuscitation care, including therapeutic hypothermia. Important current initiatives to improve cardiac arrest survival include hands-only CPR delivered by laypersons prior to the arrival of EMS, dispatcher-assisted CPR and implementation of hospital-based therapeutic hypothermia protocols to improve postresuscitation care. Optimizing cardiac arrest survival requires a team effort among all providers of acute cardiac care in the out-of-hospital and in-hospital settings. A coordinated initiative based upon a seamless implementation of the chain of survival can improve survival for victims of sudden cardiac arrest.

References

1. U.S. Census Bureau, Census 2000: Summary File 1. Available at http://www.census.gov. Accessed November 13, 2007.
2. Chugh SS, Jui J, Gunson K, Stecker EC, John BT, Thompson B, Ilias N, Vickers C, Dogra V, Daya M, Kron J, Zheng Z-J, Mensah G, McAnulty J: Current burden of sudden cardiac death: Multiple source surveillance versus retrospective death certificate-based review in a large U.S. community. J Am Coll Cardiol 2004;44:1268-1275.
3. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, Rea T, Lowe R, Brown T, Dreyer J, Davis D, Idris A, Stiell I: Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA 2008;300:1423-1431.
4. Agarwal DA, Hess EP, Atkinson EJ, White RD: Ventricular fibrillation in Rochester, Minnesota: Experience over 18 years. Resuscitation 2009;80:1253-1258.
5. Rea TD, Helbock M, Perry S, Garcia M, Cloyd D, Becker L, Eisenberg M: Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: Survival implications of guideline changes. Circulation 2006;114:2760-2765.
6. Eisenberg M, White RD: The unacceptable disparity in cardiac arrest survival among American communities. Ann Emerg Med 2009;54:258-260.
7. Cummins RO, Ornato JP, Thies WH, Pepe PE: Improving survival from sudden cardiac arrest: The "chain of survival" concept. A statement for health professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. Circulation 1991;83:1832-1847.
8. White RD, Bunch TJ, Hankins DG: Evolution of a community-wide early defibrillation programme experience over 13 years using police/fire personnel and paramedics as responders. Resuscitation 2005;65:279-283.
9. Stiell IG, Wells GA, DeMaio VJ, Spaite DW, Field BJ 3rd, Munkley DP, Lyver MB, Luinstra LG, Ward R: Modifiable factors associated with improved cardiac arrest survival in a multicenter basic life support/defibrillation system: OPALS Study Phase I results. Ontario Prehospital Advanced Life Support. Ann Emerg Med 1999;33:44-50.
10. Sasson C, Rogers MAM, Dahl J, Kellermann AL: Predictors of survival from out-of-hospital cardiac arrest: A systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2010;3:63-81.
11. Campbell RL, Hess EP, Atkinson EJ, White RD: Assessment of a three-phase model of out-of-hospital cardiac arrest in patients with ventricular fibrillation. Resuscitation 2007;73:229-235.
12. Rea TD, Eisenberg MS, Culley LL, Becker L: Dispatcher-assisted cardiopulmonary resuscitation and survival in cardiac arrest. Circulation 2001;104:2513-2516.
13. International Liaison Committee on Resuscitation. 2005 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Circulation 2005;112(suppl IV):IV-12-IV-18.
14. 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;40:553-562.
15. Abella BS, Alvarado JP, Myklebust H, Edelson DP, Barry A, O'Hearn N, Vanden Hoek TL, Becker LB: Quality of cardiopulmonary resuscitation during in-hospital cardiac arrest. JAMA 2005;293:305-310.
16. Wik L, Kramer-Johansen J, Myklebust H, Sorebo H, Svensson L, Fellows B, Steen PA: Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest. JAMA 2005;293:299-304.
17. Christenson J, Andrusiek D, Everson-Stewart S, Kudenchuk P, Hostler D, Powell J, Callaway CW, Bishop D, Vaillancourt C, Davis D, Aufderheide TP, Idris A, Stouffer JA, Stiell I, Berg R, Resuscitation Outcomes Consortium I: Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. Circulation 2009;120:1241-1247.
18. Sayre MR, Berg RA, Cave DM, Page RL, Potts J, White RD, American Heart Association Emergency Cardiovascular Care C: 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;117:2162-2167.
19. Group S-Ks: Cardiopulmonary resuscitation by bystanders with chest compression only (SOS-KANTO): An observational study. Lancet 2007;369:920-926.
20. Iwami T, Kawamura T, Hiraide A, Berg RA, Hayashi Y, Nishiuchi T, Kajino K, Yonemoto N, Yukioka H, Sugimoto H, Kakuchi H, Sase K, Yokoyama H, Nonogi H: Effectiveness of bystander-initiated cardiac-only resuscitation for patients with out-of-hospital cardiac arrest. Circulation 2007;116:2900-2907.
21. Bohm K, Rosenqvist M, Herlitz J, Hollenberg J, Svensson L: Survival is similar after standard treatment and chest compression only in out-of-hospital bystander cardiopulmonary resuscitation. Circulation 2007;116:2908-2912.
22. Ong ME, Ng FS, Anushia P, Tham LP, Leong BS, Ong VY, Tiah L, Lim SH, Anantharaman V: Comparison of chest compression only and standard cardiopulmonary resuscitation for out-of-hospital cardiac arrest in Singapore. Resuscitation 2008;78:119-126.
23. Snyder DE, White RD, Jorgenson DB: Outcome prediction for guidance of initial resuscitation protocol: Shock first or CPR first. Resuscitation 2007;72:45-51.
24. Weisfeldt ML, Becker LB: Resuscitation after cardiac arrest: A 3-phase time-sensitive model. JAMA 2002;288:3035-3038.
25. Cobb LA, Fahrenbruch CE, Walsh TR, Copass MK, Olsufka M, Breskin M, Hallstrom AP: Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. JAMA 1999;281:1182-1188.
26. Wik L, Hansen TB, Fylling F, Steen T, Vaagenes P, Auestad BH, Steen PA: Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: A randomized trial. JAMA 2003;289:1389-1395.
27. International Liaison Committee on Resuscitation. 2005 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Circulation 2005;112(suppl III):IV-35-IV-36.
28. Jacobs IG, Finn JC, Oxer HF, Jelinek GA: CPR before defibrillation in out-of-hospital cardiac arrest: A randomized trial. Emerg Med Australas 2005;17:39-45.
29. Baker PW, Conway J, Cotton C, Ashby DT, Smyth J, Woodman RJ, Grantham H, Clinical I: Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by

paramedics to be in ventricular fibrillation? A randomised control trial. Resuscitation 2008;79:424-431.
30. Tang W, Snyder D, Wang J, Huang L, Chang YT, Sun S, Weil MH: One-shock versus three-shock defibrillation protocol significantly improves outcome in a porcine model of prolonged ventricular fibrillation cardiac arrest. Circulation 2006;113:2683-2689.
31. Eftestol T, Sunde K, Steen PA: Effects of interrupting precordial compressions on the calculated probability of defibrillation success during out-of-hospital cardiac arrest. Circulation 2002;105:2270-2273.
32. Stiell IG, Walker RG, Nesbitt LP, Chapman FW, Cousineau D, Christenson J, Bradford P, Sookram S, Berringer R, Lank P, Wells GA: BIPHASIC Trial: A randomized comparison of fixed lower versus escalating higher energy levels for defibrillation in out-of-hospital cardiac arrest. Circulation 2007;115:1511-1517.
33. Hess EP, Russell JK, Liu PY, White RD: A high peak current 150-J fixed-energy defibrillation protocol treats recurrent ventricular fibrillation (VF) as effectively as initial VF. Resuscitation 2008;79:28-33.
34. Lindner KH, Dirks B, Strohmenger HU, Prengel AW, Lindner IM, Lurie KG: Randomised comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation. Lancet 1997;349:535-537.
35. Aung K, Htay T: Vasopressin for cardiac arrest: A systematic review and meta-analysis. Arch Intern Med 2005;165:17-24.
36. Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, Hallstrom AP, Murray WA, Olsufka M, Walsh T: Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. N Engl J Med 1999;341:871-878.
37. 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;302:2222-2229.
38. Stiell IG, Wells GA, Field B, Spaite DW, Nesbitt LP, De Maio VJ, Nichol G, Cousineau D, Blackburn J, Munkley D, Luinstra-Toohey L, Campeau T, Dagnone E, Lyver M, Ontario Prehospital Advanced Life Support Study G: Advanced cardiac life support in out-of-hospital cardiac arrest. N Engl J Med 2004;351:647-656.
39. Paradis NA, Halperin HR, Kern KB, Wenzel V, Chamberlain DA: *Cardiac Arrest: The Science and Practice of Resuscitation Medicine*, 2nd ed. New York: Cambridge University Press, 2008.
40. Arrich J, Holzer M, Herkner H, Mullner M: Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation. Cochrane Database Syst Rev 2009:CD004128.
41. Merchant RM, Soar J, Skrifvars MB, Silfvast T, Edelson DP, Ahmad F, Huang KN, Khan M, Vanden Hoek TL, Becker LB, Abella BS: Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest. Crit Care Med 2006;34:1935-1940.
42. Spaite DW, Stiell IG, Bobrow BJ, de Boer M, Maloney J, Denninghoff K, Vadeboncoeur TF, Dreyer J, Wells GA: Effect of transport interval on out-of-hospital cardiac arrest survival in the OPALS study: Implications for triaging patients to specialized cardiac arrest centers. Ann Emerg Med 2009;54:248-255.