

# Out-of-Hospital Cardiac Arrest

Tanner S. Boyd, MD<sup>a,\*</sup>, Debra G. Perina, MD<sup>b</sup>

## KEYWORDS

• Prehospital • Out-of-hospital • Cardiac arrest • Resuscitation

## ACCESS AND PRESENTATION

Emergency medical services (EMS) medical care has changed significantly since its inception. Initially, ambulances functioned merely as transport vehicles. Today, EMS has matured into an integrated part of the health care system, with the ability to provide advanced care en-route to a hospital. Regional dispatch centers now decide which resources should respond to an emergency call. EMS dispatchers are trained in emergency medical dispatch techniques and can provide prearrival instructions to bystanders, thereby expediting initial first aid and cardiopulmonary resuscitation (CPR).

Historically, much of the medical care provided by EMS grew out of traditional practice with little scientific basis. Today, in mature EMS systems, rigorous research studies are being completed and evidence-based medicine concepts used to determine proven benefit before introduction of new procedures, drugs, and adjuncts to out-of-hospital care. A research base for EMS practice now exists, a large component of which is related to out-of-hospital cardiac arrest (OHCA) techniques and therapies to improve survival. Current research is ongoing to evaluate the best treatment options for patients with OHCA.

Emphasis is placed on layperson education and all level of provider courses to rapidly access the emergency system in cases of OHCA to receive appropriate treatment. The patient (before arrest) or a witness or bystander must first recognize the problem and activate the EMS system. The more rapid this activation occurs, the more rapidly definitive care can arrive to the OHCA situation. Delays in arrival affect ultimate outcomes. Depending on the circumstances surrounding the presentation, delays can frequently occur. Cardiac arrests witnessed by bystanders or that which occur in a public area result in EMS being accessed more rapidly than in an unwitnessed event.<sup>1</sup> A Swedish study found that a period of activation of less than 4 minutes

---

The authors have nothing to disclose.

<sup>a</sup> Emergency Medicine Residency, Department of Emergency Medicine, University of Virginia School of Medicine, University of Virginia, PO Box 800699, Charlottesville, VA 22908, USA

<sup>b</sup> Division of Prehospital Care, Department of Emergency Medicine, University of Virginia School of Medicine, University of Virginia, PO Box 800699, Charlottesville, VA 22908, USA

\* Corresponding author.

E-mail address: [tanner.boyd@gmail.com](mailto:tanner.boyd@gmail.com)

Emerg Med Clin N Am 30 (2012) 13–23

doi:[10.1016/j.emc.2011.09.004](https://doi.org/10.1016/j.emc.2011.09.004)

[emed.theclinics.com](http://emed.theclinics.com)

0733-8627/12/\$ – see front matter © 2012 Elsevier Inc. All rights reserved.

from time of cardiac arrest to EMS activation increased the 1-month survival rate from 2.8% to 6.9% ( $P < .0001$ ).<sup>2</sup> Likewise, more rapid EMS response times<sup>3</sup> and shorter times to CPR initiation increase overall survival. The same conditions can also be extrapolated to traumatic cardiac arrests as well, although outcome in such settings is less optimal.

Delays in accessing care can also occur in patients with chest pain who are at high risk for OHCA or in a prearrest state. One of the largest randomized trials to date addressing delays in treatment to patients experiencing chest pain is the European Myocardial Infarction Project.<sup>4</sup> Collecting data from 15 European countries and Canada between 1988 and 1992, this study found the largest delays occurred in female patients, those older than 65 years, those who had experienced chest pain in the previous 24 hours, and those with pulmonary edema. Characteristics of patients with the shortest delay to summoning an ambulance included those with a history of previous myocardial infarction (MI), those in shock, and those experiencing ventricular fibrillation.

These factors associated with delays to EMS activation were also noted again in numerous smaller studies with the addition of other factors such as lower socioeconomic status, a family member being present at symptom onset, and the belief that symptoms were not severe enough to summon EMS. Some studies suggest increased frequency of atypical symptoms in women causing a larger time gap between onset of symptoms and access of care,<sup>5</sup> whereas others show no gender difference at all.<sup>6</sup> A large Swedish study reviewing demographics of patients with acute MI over 15 years found that before the age of 65 years, there was no gender difference in hospital delay. However, after 65 years of age, there was an increased time delay for women.<sup>7</sup>

Adding to delay in access to care, certain populations can present without chest pain at all and suddenly experience OHCA. Elderly and diabetic patients may have atypical presentations of acute MI with nonspecific symptoms such as dizziness, syncope, malaise, nausea, vomiting, or abdominal pain. Patients experiencing a significant cardiac or prearrest event may also present with congestive heart failure, hypotension, or severe respiratory distress. These presentations not only can cause delays in access of care but also may mislead health care personnel, causing a delay in recognition of the prearrest setting that can degenerate into OHCA if not properly recognized and treated promptly.

Ready access to automated external defibrillator (AED) devices that can rapidly analyze and deliver electrical shocks if indicated should also be part of the overall community strategy to decrease delays in access to care. Strategies for optimal survival of patients with OHCA include minimizing delays in accessing care, proper placement of AEDs in locations where patients with OHCA may be more likely encountered, and dispatch call centers staffed by trained emergency dispatchers who use prearrival instructions to begin bystander care and CPR before EMS arrival. Public awareness, lay provider education campaigns, CPR AED instruction, and encouragement to use the EMS system all play important roles in the ultimate reduction in the access to care.

## DEMOGRAPHICS

It is estimated that more than 166,000 patients experience OHCA each year.<sup>8</sup> Several historical risk factors have been associated with OHCA. A diagnosis of congestive heart failure carried an OHCA incidence of 21.87 per 1000 subject years, whereas a history of diabetes mellitus, previous MI, smoking, and hypertension resulted in incidences of 13.80, 13.69, 9.18, and 7.54, respectively.<sup>9</sup> Cardiac arrests, along with MIs

and unstable angina, seem to have a circadian variation, with a morning peak after the initiation of daily activities.<sup>10</sup> EMS response to patients with OHCA seems to be more frequent during this period as well.

A well-defined body of resuscitation literature has reported that survivors of cardiac arrest have a greater chance of successful resuscitation if the presenting rhythm is shockable and the least likelihood if the presenting rhythm is asystole. Patients with OHCA have been reported to have initial rhythms of ventricular tachycardia, ventricular fibrillation, or a shockable rhythm as determined by an AED 23% of the time. Another 9% of patients with OHCA had nonshockable rhythms per AED, with 40% showing asystole, 20% pulseless electrical activity (PEA), and the final 9% being unknown or undetermined rhythms.<sup>11</sup> OHCA research suffered from the lack of a consistent definition of cardiac arrest and poor reporting across EMS services until the creation and adoption of the uniform data collection and reporting criteria, Utstein criteria, which now allow researchers to nationally pool data and perform comparisons across services.<sup>12</sup> OHCA rates show a wide variation with the overall incidence calculated, using the uniform criteria, to be 95 per 100,000 subject-years.

## OHCA OUTCOMES

It is estimated that more than 166,000 patients experience OHCA each year. This public health condition has defined a research agenda to identify effective treatments and strategies that could result in increased survival rates. Despite efforts, OHCA survival rates remain bleak. Before adoption of the Utstein criteria, outcomes in patients with OHCA were difficult to measure secondary to the lack of standardization of variables between EMS systems. Some of these variables included pulse presence on arrival to the emergency department (ED), general return of circulation, and definition of what constitutes patient survival. This inconsistency led to the 1995 adoption of uniform definitions, data collection sets, and reporting with the use of the Utstein criteria that has allowed greater standardization and comparison between research studies.<sup>12</sup> Despite this, comparison of research data is still hampered by differences in EMS systems, response times, patient downtimes, and bystander CPR and AED availability.

Despite research limitations, several factors seem to be associated with an increased chance of survival in OHCA. Bystander CPR, witnessed arrest, initial presenting rhythm of ventricular fibrillation, and short response times to defibrillation are all associated with increased survival rates.<sup>13,14</sup> Eisenburger and colleagues<sup>15</sup> also showed that having a cardiac arrest in a public place was an independent predictor of improved outcome. Immediate defibrillation of patients in ventricular fibrillation results in a pulse-generating rhythm and survival to hospital discharge in 56% of patients. This decreases, with each successive defibrillation attempt eventually reaching 6% by the third attempt. Survival rates have been shown to be at their highest if defibrillation occurs within the first 6 minutes of cardiac arrest, decreasing as the interval increases up to 11 minutes, and leveling off after that time.<sup>15</sup>

There is a large degree of variability reported in OHCA survival ranges, with a low of 6% and a high of 46%. However, the largest cumulative meta-analysis study to date documented a mean survival to hospital discharge for all rhythm groups of only 7.6% and a hospital admission rate of only 23.8%.<sup>16</sup> This outcome variability is attributable to the factors previously mentioned in addition to local population characteristics and other factors. Liu and colleagues<sup>17</sup> reported that younger age, nonwhite race, and male gender were associated with better outcomes. Time of EMS arrival is linked to higher survival rates, with even a 1-minute decrease in mean response times showing

an approximate 1% (0.7%–2.1% range) absolute increase in survival. In addition to response times, decreasing overall pauses in CPR is associated with better results.<sup>18</sup> EMS-witnessed cardiac arrests seem to have the best outcomes followed by bystander-witnessed arrests with bystander CPR, bystander-witnessed arrests without bystander CPR, and unwitnessed arrests.<sup>19</sup>

The benefits of advanced life support (ALS) versus basic life support (BLS) on cardiac arrest outcomes have been questioned by some. The largest study to date, the Ontario Prehospital Advanced Life Support study, looked at the effects of multiple EMS variables on OHCA outcomes as ALS was phased into their EMS system. In phase 1 of this study, age, witnessed arrest, bystander CPR, CPR by fire or police, and short EMS response times were independently associated with survival in multivariate analysis.<sup>20</sup> In phase 2, a target of 8 minutes was set for the time from call receipt to response on scene with a defibrillator. Of the 1641 patients with cardiac arrest in the study, 90% of calls met this target with a 33% improvement in overall survival to discharge in all rhythm groups. This response time was estimated to save an additional 21 lives at a cost of \$2400 per life.<sup>14</sup> When all patients were analyzed, there were a total of 1391 patients who were enrolled in the defibrillation plus BLS phase of the study and another 4247 patients enrolled in the advanced cardiac life support (ACLS) phase. The population with ACLS had greater return of spontaneous circulation (ROSC) rates (12.9% vs 18.0%,  $P < .001$ ) and survival to hospital admission rates (10.9% vs 14.6%,  $P < .001$ ), but hospital discharge rates were unchanged (5.0% vs 5.1%;  $P = .83$ ). This rate led to an odds ratio of 1.1 for ACLS relative to BLS. This rate did not relate favorably to the odds ratios of 4.4, 3.7, and 3.4 for witnessed arrest, early CPR, and early defibrillation, respectively, in achieving meaningful impact of OHCA survival rates.<sup>21</sup>

Another study comparing prehospital ACLS in OHCA with and without intravenous (IV) medications found no difference in ROSC, survival to hospital admission, or hospital discharge among shockable rhythm groups. However, if the initial rhythm was PEA or asystole, the IV group had better rates of ROSC (29% vs 11%,  $P < .001$ ) and survival to hospital admission (31% vs 16%,  $P < .001$ ) but not to hospital discharge (2% vs 3%,  $P = .65$ ).<sup>22</sup> This finding of lack of ALS impact on hospital discharge rates was not supported in a meta-analysis of 37 articles from 1999 describing 39 EMS systems and 33,124 patients. This study reported the odds ratio of survival to hospital discharge for BLS plus defibrillation systems to be 1.71 (95% confidence interval [CI], 1.09–2.70;  $P = .01$ ) for ACLS, 1.47 (95% CI, 0.89–2.42;  $P = .07$ ) for 2-tiered BLS and ALS systems, and 2.31 (95% CI, 1.47–3.62;  $P < .01$ ) for 2-tiered BLS with defibrillation and ALS systems. This study was not sufficiently powered to demonstrate whether 1- or 2-tiered systems had better survival rates but was able to show that ALS is more effective than BLS plus defibrillation alone.<sup>13</sup> Regardless of whether one believes the data showing no benefit in hospital discharge with ACLS or favors the studies showing some improvement, both studies reported that ACLS improves survival to hospital admission and ROSC in the out-of-hospital setting.

Hospital destination for survivors of OHCA also seems to influence outcomes. Lui and colleagues<sup>17</sup> reported that hospital survival rates varied among hospitals from 29% to 42% despite identical EMS treatment. Another study also showed that outcomes at designated critical care medical centers are better.<sup>23</sup> Callaway and colleagues<sup>24</sup> found that hospitals with cardiac catheterization capability that come across at least 40 cardiac arrests per year have better outcomes, regardless of how many beds are in the hospital or whether it is considered a teaching hospital or not. Patients with cardiac arrests caused by ST elevation MIs who arrive at the ED with ROSC generally have better outcomes.<sup>25</sup> Surprisingly, higher survival rates are not

limited to urban areas alone because rural locations have also documented neurologically intact survival to hospital discharge rates as high as 22%.

When to terminate out-of-hospital resuscitation efforts is still a topic of controversy with the wish to not prolong efforts beyond potential benefit along with the possibility of neurologic devastation weighed against the desire to not declare death prematurely. Concern for the safety and well-being of both EMS providers and the public because of the rate of ambulance accidents when running with lights and sirens, benched against the lack of proved benefit of transport of patients with OHCA without ROSC, has led to general acceptance of termination of resuscitation efforts in the field. Multiple rules have been validated for the termination of prehospital CPR, with the most popular one resulted from methodology that determined only 46% of cardiac arrests needed transportation.<sup>26</sup> This rule states that if there is no ROSC after 3 rounds of BLS with defibrillation pauses every 1 to 2 minutes, if no shock was delivered by an AED, and if the cardiac arrest was unwitnessed by an emergency medical technician or firefighter, then all resuscitation efforts may be terminated.<sup>26</sup> When validated, this rule had a sensitivity of 57.5% to 64.4%, a specificity of 90.2% to 100.0%, and a positive predictive value of 99.5% to 100.0%.<sup>26,27</sup> When neurologic status was factored in, this rule correctly identified 100% of those discharged with good neurologic outcome and 36% of those with poor neurologic outcome or who did not survive.<sup>28</sup> Although some EMS systems have enacted this, others prefer to make decisions on a per-case basis. Individual case factors that may lead to transportation despite this validated termination rule are airway difficulties, persistent ventricular dysrhythmias, excessively public location, family members who are unable to accept field termination, lack of IV cannulation, and cultural or language barriers. In addition, many emergency physicians do not feel comfortable pronouncing a PEA code in the field. Regardless of the decision to transport or terminate efforts at the scene, family members are generally accepting of termination in cases of unsuccessful out-of-hospital resuscitation efforts.

OHCAs can also be traumatic in origin. Patients with this condition have an extremely high mortality rate, with survivors having significant morbidity. However, as with medical cardiac arrests, research suggests that a small subset of these patients can potentially benefit from timely aggressive treatment. Studies looking at the impact of EMS care concluded that any intervention that delays a patient's hospital arrival has a negative impact on survival in the trauma patient. Although resuscitative thoracotomy is a possibility in the setting of traumatic cardiac arrests to allow for open cardiac massage, pericardiectomy for tamponade release, cardiac/aortic penetration occlusion, or descending aortic cross-clamping until definitive repair, this procedure only applies to a small subset of patients. These patients include those in arrest less than 4 minutes before ED arrival, those with signs of life on ED arrival, or those with suspected pericardial tamponade leading to arrest. Prognosis is dismal in those without signs of life on ED arrival and in patients with asystolic or bradycardic rhythms; resuscitative thoracotomy is generally not recommended.

## RESPONSE SYSTEMS AND PROCESS

To improve cardiac arrest outcomes, each link in the chain of survival must be optimized. In the prehospital world, this optimization includes the prompt identification of a cardiac arrest, proper dispatch of care, rapid initiation of CPR, immediate defibrillation, high-quality CPR, and rapid transport to the most appropriate hospital. Public education campaigns continue to improve awareness of cardiac arrest signs and symptoms, but there is little that can be done to improve outcomes unless the emergency response system is activated.

The first person a caller speaks with when calling 911 is a trained dispatcher. Outcomes have been shown to be better when dispatchers receive more frequent cardiac arrest calls.<sup>29</sup> Unfortunately, any sign of breathing, including agonal breathing, decreases the chances that a dispatcher will recognize a cardiac arrest.<sup>30</sup> However, teaching dispatchers to recognize agonal breathing increases not only the detection of cardiac arrests<sup>31</sup> but also the frequency with which CPR instructions are given.<sup>32</sup> To help dispatchers, computer systems have been developed to assist in the detection of OHCA. The Medical Priority Dispatch System has been shown to have a sensitivity of 76.7% and a specificity of 99.2% at detecting a cardiac arrest.<sup>33</sup> Likewise, the Advanced Medical Priority Dispatch System increased the number of people accurately identified as being in cardiac arrest compared with dispatchers alone.<sup>34</sup> Despite these guides, it is clear that these computer systems continue to misidentify patients with OHCA, and, thus, there is still room for improvement in dispatcher detection of cardiac arrests.

Once a cardiac arrest is identified, dispatchers can then give CPR instructions to a bystander over the phone until further help arrives. Telephone instructions have been shown to increase the rates of bystander CPR<sup>35</sup> and enhance outcomes.<sup>29</sup> A simulation study showed that a lay volunteer, without any training in CPR, can do compressions just as well with phone instructions as a previously trained person without directions. This finding is easily extrapolated into the real world because some compressions are better than no compressions. Only 2% of witnesses to a cardiac arrest refuse to do CPR.<sup>30</sup> When receiving instructions, directions to put the phone down during chest compressions do not improve CPR quality.<sup>36</sup> With the advent of widespread cell phones, there is ongoing research using video calls to help dispatchers aid bystanders in CPR instructions.<sup>37</sup>

Studies have also shown that the time to initiation of chest compressions is more rapid if the caller is given hands-only instructions (ie, no rescue breaths) rather than standard CPR instructions.<sup>38</sup> Given the possibility that hands-only CPR could improve outcomes, 2 recent articles in the *New England Journal of Medicine* compared the new technique to standard CPR with ventilations. In one study, there was a trend, although not statistically significant, toward increased rates of survival to hospital discharge with hands-only CPR in the subgroups with a cardiac cause of OHCA (15.5% vs 12.3%,  $P = .09$ ) and with a shockable rhythm (31.9% vs 25.7%,  $P = .09$ ).<sup>39</sup> Another study reported a slightly more positive trend to hospital discharge (19.1% vs 14.7%,  $P = .16$ ) but no change in 30-day mortality (8.7% vs 7.0%,  $P = .26$ ).<sup>40</sup> With no apparent harm and possible benefit in providing hands-only CPR instructions, recently released American Heart Association guidelines call for compression-only CPR in the initial management of cardiac arrest. This recommendation is particularly relevant to dispatcher phone instructions because of the relative ease of remotely guiding someone through compression-only CPR.

As time to first defibrillation has been shown to positively affect outcomes in OHCA, a variety of methods have been developed to increase the speed with which someone in a shockable rhythm is defibrillated. The development of AEDs has given the lay public access to easy-to-use lifesaving interventions. AEDs have been widely placed in strategic locations, including public locations to facilitate more rapid defibrillation of the cardiac arrest patient. In addition, law enforcement officers, firefighters, and other first responders in many communities carry AEDs. Approximately 80% of police departments are used as first responders to medical events; of these law enforcement first responders, 39% carry AEDs. In general, 31% of police departments carry AEDs.<sup>41</sup>

High-quality uninterrupted chest compressions have been correlated with increased survival rates. Various devices have been created to increase the quality of

compressions. Pressure-sensing devices placed between the chest and a provider's hands give real-time feedback to improve the quality of compressions. Mechanical devices that replace EMS providers may give more consistent compressions and free providers for other tasks in the resuscitation process.

Another innovation in methods of CPR is the concept of cardiocerebral resuscitation (CCR). CCR aims to improve outcomes through refocusing certain interventions in CPR to maximize myocardial and cerebral perfusion. In CCR, chest compressions are started immediately and continued for 200 continuous compressions. During this time, oxygen is given via a noninvasive airway (ie, no endotracheal intubation), and defibrillator pads are placed on the patient. The rhythm is analyzed, and, when appropriate, a shock is given followed immediately by another interval of 200 compressions without pulse check. Epinephrine is given early, and endotracheal intubation is delayed until after 3 rounds of chest compressions are completed.<sup>42</sup> Some have modified CCR by intubating earlier if the initial rhythm is not shockable.<sup>43</sup> Although much research is still underway regarding CCR, the early data is favorable. One study designed as a before-and-after intervention introducing CCR into an EMS system while all other factors remained constant reported that the rate of those who survived to discharge increased (47% vs 20%;  $P =$  not reported) and the total number of patients neurologically intact (39% vs 15%;  $P =$  not reported) increased.<sup>44</sup> Another study reported that the overall adjusted odds ratio of survival for CCR was 3.1 (95% CI, 1.96–4.76), with some age ranges improving more than others. All age ranges except for 70 to 79 years reached significance in their confidence intervals.<sup>45</sup> When the first 3 years of this data was presented in percentages, CCR showed a survival to hospital discharge increase of 5.4% versus 1.8% ( $P =$  not reported).<sup>42</sup> Despite much promise, this new method of CPR requires further ongoing study.

When ROSC occurs, it is vital to transport the patient to the most appropriate hospital rapidly. However, transport provides its own pitfalls to a pulseless patient still undergoing active resuscitation. Although compression quality en-route was equivalent in one study, hands-off time increased during transport when compared with on-scene resuscitation.<sup>44</sup> Another study showed that the efficiency of chest compressions, relative to being on scene, were 95% in a moving ambulance and 86% in a helicopter.<sup>46</sup> The rate and quality of chest compressions have been shown to increase as the speed of an ambulance increased.<sup>47</sup> Use of lights and sirens en-route to a hospital saved a mean of 2.62 minutes, yet only 4.5% of patients received time-critical interventions, none of which occurred during the specific time saved.<sup>48</sup> Given the risk of priority EMS transport to both providers and the public, consideration should be given to mitigate the use of lights as sirens unless absolutely necessary because minimal benefit has been shown by doing so. Longer transport times were not associated with increased survival, thereby calling for more research into bypassing smaller hospitals and taking patients directly to a regionally designated resuscitation hospital<sup>49,50</sup>; this issue is being thoroughly reviewed at this time with conflicting evidence noted for and against such transportation strategies. At present, patients who have undergone resuscitation are often taken to the closest hospital, stabilized, and then transferred to a larger more-specialized hospital. For these interfacility transports, specialized critical care ground or air transport units are often used that include a combination of advanced EMS providers, critical care nurses, or physicians. These services can provide specialized care options such as vasoactive drug administration, blood product transfusions, intra-aortic balloon pumps, ventilator management, and so forth. Despite the criticality of the patients transported, rearrest occurs while being transported to a tertiary care facility in a minority of patients with cardiac arrest who have undergone resuscitation.<sup>51</sup>

For those patients with ROSC, studies using therapeutic hypothermia have been promising. The definitive studies were conducted in Europe and Australia with therapeutic hypothermia showing benefit for those patients presenting with ventricular fibrillation, who remained in a coma, and who did not have persistent hypotension while being cooled to the target range within 4 hours of ROSC.<sup>52</sup> The current American Heart Association consensus guidelines call for such patients to be cooled as soon as possible but within 4 hours of ROSC to a core body temperature between 32°C and 34°C. This cooling can be accomplished on-scene or en-route by cooling of the patient with 2 L of ice-cold normal saline or lactated Ringer solution. No studies to date have shown that initiation of cooling by EMS improves either hospital discharge rates or neurologic function compared with cooling after arrival in the ED.<sup>53</sup> Further study is needed in this regard.

## SUMMARY

Despite research and advances in cardiac arrest resuscitation, outcomes have not changed appreciatively in nearly 3 decades, remaining dismal in most areas of the United States.<sup>16</sup> With a renewed focus on maximizing each link in the chain of survival, short-term outcomes (eg, ROSC and survival to hospital admission) are slowly increasing. Education is making the public more knowledgeable and able to recognize and provide prompt attention to patients in whom OHCA occurs. Studies bear out that improvements in EMS dispatch, response times, and more rapid defibrillation times have had an impact, albeit small, producing better outcomes. Standardization and use of the Utstein criteria have allowed higher-quality research to be conducted on patients with OHCA. Continued advancement in ACLS care gives us the hope of further improving outcomes. Regardless, further study is needed in all aspects of OHCA treatments if we are to meaningfully improve survival of such patients. There is still opportunity to improve each link in the OHCA chain of survival.

## REFERENCES

1. Swor RA, Compton S, Domeier R, et al. Delay prior to calling 9-1-1 is associated with increased mortality after out-of-hospital cardiac arrest. *Prehosp Emerg Care* 2008;12(3):333–8.
2. Herlitz J, Engdahl J, Svensson L, et al. A short delay from out of hospital cardiac arrest to call for ambulance increases survival. *Eur Heart J* 2003;24(19):1750–5.
3. Vukmir RB. Survival from prehospital cardiac arrest is critically dependent upon response time. *Resuscitation* 2006;69(2):229–34.
4. Leizorovicz A, Haugh MC, Mercier C, et al. Pre-hospital and hospital time delays in thrombolytic treatment in patients with suspected acute myocardial infarction. Analysis of data from the EMIP study. European Myocardial Infarction Project. *Eur Heart J* 1997;18(2):248–53.
5. Ottesen MM, Dixen U, Torp-Pedersen C, et al. Prehospital delay in acute coronary syndrome—an analysis of the components of delay. *Int J Cardiol* 2004;96(1):97–103.
6. Moser DK, McKinley S, Dracup K, et al. Gender differences in reasons patients delay in seeking treatment for acute myocardial infarction symptoms. *Patient Educ Couns* 2005;56(1):45–54.
7. Isaksson RM, Holmgren L, Lundblad D, et al. Time trends in symptoms and pre-hospital delay time in women vs. men with myocardial infarction over a 15-year period. The Northern Sweden MONICA Study. *Eur J Cardiovasc Nurs* 2008;7(2):152–8.

8. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics—2008 update: report from the American Heart Association Statistics Committee and Strokes Statistics Subcommittee. *Circulation* 2008;117(4):e25–146.
9. Rea TD, Pearce RM, Raghunathan TE, et al. Incidence of out-of-hospital cardiac arrest. *Am J Cardiol* 2004;93(12):1455–60.
10. Muller JE. Circadian variation in cardiovascular events. *Am J Hypertens* 1999; 12(2 Pt 2):35S–42S.
11. Lindholm DJ, Campbell JP. Predicting survival from out-of-hospital cardiac arrest. *Prehosp Disaster Med* 1998;12(2–4):51–4.
12. Spaite D, Benoit R, Brown D, et al. Uniform prehospital data elements and definitions: a report from the uniform prehospital emergency medical services data conference. *Ann Emerg Med* 1995;25(4):525–34.
13. Nichol G, Stiell IG, Laupacis A, et al. 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.
14. Stiell IG, Wells GA, Field BJ, et al. Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS study phase II. Ontario Prehospital Advanced Life Support. *JAMA* 1999;281(13): 1175–81.
15. Eisenburger P, Sterz F, Haugk M, et al. Cardiac arrest in public locations—an independent predictor for better outcome? *Resuscitation* 2006;70(3):395–403.
16. Sasson C, Rogers MA, Dahl J, et 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.
17. Liu JM, Yang Q, Pirralo RG, et al. Hospital variability of out-of-hospital cardiac arrest survival. *Prehosp Emerg Care* 2008;12(3):339–46.
18. Lund-Kordahl I, Olasveengen TM, Lorem T, et al. Improving outcome after out-of-hospital cardiac arrest by strengthening weak links of the local Chain of Survival; quality of advanced life support and post-resuscitation care. *Resuscitation* 2010; 81(4):422–6.
19. Hostler D, Thomas EG, Emerson SS, et al. Increased survival after EMS witnessed cardiac arrest. Observations from the Resuscitation Outcomes Consortium (ROC) Epistry—Cardiac arrest. *Resuscitation* 2010;81(7):826–30.
20. Stiell IG, Wells GA, DeMaio VJ, et al. 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(1):44–50.
21. 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):647–56.
22. Olasveengen TM, Sunde K, Brunborg C, et al. Intravenous drug administration during out-of-hospital cardiac arrest: a randomized trial. *JAMA* 2009;302(20): 2222–9.
23. Kajino K, Iwami T, Daya M, et al. Impact of transport to critical care medical centers on outcomes after out-of-hospital cardiac arrest. *Resuscitation* 2010; 81(5):549–54.
24. Callaway CW, Schmicker R, Kampmeyer M, et al. Receiving hospital characteristics associated with survival after out-of-hospital cardiac arrest. *Resuscitation* 2010;81(5):524–9.
25. Pleskot M, Hazukova R, Stritecka H, et al. Long-term prognosis after out-of-hospital cardiac arrest with/without ST elevation myocardial infarction. *Resuscitation* 2009;80(7):795–804.

26. Morrison LJ, Verbeek PR, Zhan C, et al. Validation of a universal prehospital termination of resuscitation clinical prediction rule for advanced and basic life support providers. *Resuscitation* 2009;80(3):324–8.
27. Morrison LJ, Visentin LM, Kiss A, et al. Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. *N Engl J Med* 2006;355(5):478–87.
28. Ruygrok ML, Byyny RL, Haukoos JS, et al. Validation of 3 termination of resuscitation criteria for good neurologic survival after out-of-hospital cardiac arrest. *Ann Emerg Med* 2009;54(2):239–47.
29. Kuisma M, Boyd J, Vayrynen T, et al. Emergency call processing and survival from out-of-hospital ventricular fibrillation. *Resuscitation* 2005;67(1):89–93.
30. Bohm K, Rosenqvist M, Hollenberg J, et al. Dispatcher-assisted telephone-guided cardiopulmonary resuscitation: an underused lifesaving system. *Eur J Emerg Med* 2007;14(5):256–9.
31. Roppolo LP, Westfall A, Pepe PE, et al. Dispatcher assessments for agonal breathing improve detection of cardiac arrest. *Resuscitation* 2009;80(7):769–72.
32. Bohm K, Stalhandske B, Rosenqvist M, et al. Tuition of emergency medical dispatchers in the recognition of agonal respiration increases the use of telephone assisted CPR. *Resuscitation* 2009;80(9):1025–8.
33. Flynn J, Archer F, Morgans A. Sensitivity and specificity of the medical priority dispatch system in detecting cardiac arrest emergency calls in Melbourne. *Prehosp Disaster Med* 2006;21(2):72–6.
34. Heward A, Damiani M, Hartley-Sharpe C. Does the use of the advanced medical priority dispatch system affect cardiac arrest detection? *Emerg Med J* 2004;21(1):115–8.
35. Vaillancourt C, Verma A, Trickett J, et al. Evaluating the effectiveness of dispatch-assisted cardiopulmonary resuscitation instructions. *Acad Emerg Med* 2007;14(10):877–83.
36. Brown TB, Saini D, Pepper T, et al. Instructions to “put the phone down” do not improve the quality of bystander initiated dispatcher-assisted cardiopulmonary resuscitation. *Resuscitation* 2008;76(2):249–55.
37. Johnsen E, Bolle SR. To see or not to see—better dispatcher-assisted CPR with video-calls? A qualitative study based on simulated trials. *Resuscitation* 2008;78(3):320–6.
38. Dorph E, Wik L, Steen PA. Dispatcher-assisted cardiopulmonary resuscitation. An evaluation of efficacy amongst elderly. *Resuscitation* 2003;56(3):265–73.
39. 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.
40. 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.
41. Hawkins SC, Shapiro AH, Sever AE, et al. The role of law enforcement agencies in out-of-hospital emergency care. *Resuscitation* 2007;72(3):386–93.
42. 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(10):1158–65.
43. 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):244–52.
44. Olasveengen TM, Wik L, Steen PA. Quality of cardiopulmonary resuscitation before and during transport in out-of-hospital cardiac arrest. *Resuscitation* 2008;76(2):185–90.

45. Mosier J, Itty A, Sanders A, et al. Cardiocerebral resuscitation is associated with improved survival and neurologic outcome from out-of-hospital cardiac arrest in elders. *Acad Emerg Med* 2010;17(3):269–75.
46. Havel C, Schreiber W, Trimmel H, et al. Quality of closed chest compression on a manikin in ambulance vehicles and flying helicopters with a real time automated feedback. *Resuscitation* 2010;81(1):59–64.
47. Chung TN, Kim SW, Cho YS, et al. Effect of vehicle speed on the quality of closed-chest compression during ambulance transport. *Resuscitation* 2010;81(7):841–7.
48. Marques-Baptista A, Ohman-Strickland P, Baldino KT, et al. Utilization of warning lights and siren based on hospital time-critical interventions. *Prehosp Disaster Med* 2010;25(4):335–9.
49. 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):61–6.
50. Spaite DW, Stiell IG, Bobrow BJ, et al. 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(2):248–55.
51. Hartke A, Mumma BE, Rittenberger JC, et al. Incidence of re-arrest and critical events during prolonged transport of post-cardiac arrest patients. *Resuscitation* 2010;81(8):938–42.
52. Nolan JP, Morley T, Vanden Hoek TL, et al. Therapeutic hypothermia after cardiac arrest. *Circulation* 2003;108:118–21.
53. Bernard SA, Smith K, Cameron P, et al. Induction of therapeutic hypothermia by paramedics after resuscitation from out-of-hospital ventricular fibrillation cardiac arrest: a randomized controlled trial. *Circulation* 2010;122(7):737–42.