

Out-of-hospital cardiac arrest: 10 years of progress in research and treatment

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Cardiac disease is the most common cause of mortality in Western countries, with most deaths due to out-of-hospital cardiac arrest (OHCA). In Sweden, 5000–10 000 OHCA occur annually. During the last decade, the time from cardiac arrest to start of cardiopulmonary resuscitation (CPR) and defibrillation has increased, whereas survival has remained unchanged or even increased. Resuscitation of OHCA patients is based on the 'chain-of-survival' concept, including early (i) access, (ii) CPR, (iii) defibrillation, (iv) advanced cardiac life support and (v) post-resuscitation care. Regarding early access, agonal breathing, telephone-guided CPR and the use of 'track and trigger systems' to detect deterioration in patients' condition prior to an arrest are all important. The use of compression-only CPR by bystanders as an alternative to standard CPR in OHCA has been debated. Based on recent findings, guidelines recommend telephone-guided chest compression-only CPR for untrained rescuers, but trained personnel are still advised to give standard CPR with both compressions and ventilation, and the method of choice for this large group remains unclear and demands for

a randomized study. Data have shown the benefit of public access defibrillation for dispatched rescuers (e.g. police and fire fighters) but data are not as strong for the use of automated defibrillators (AEDs) by trained or untrained rescuers. Postresuscitation, use of therapeutic hypothermia, the importance of specific prognostic survival factors in the intensive care unit and the widespread use of percutaneous coronary intervention have all been considered. Despite progress in research and improved treatment regimens, most patients do not survive OHCA. Particular areas of interest for improving survival include (i) identification of high-risk patients prior to their arrest (e.g. early warning symptoms and genes); (ii) increased use of bystander CPR training (e.g. in schools) and simplified CPR techniques; (iii) better identification of high-incidence sites and better recruitment of AEDs (via mobile phone solutions?); (iv) improved understanding of the use of therapeutic hypothermia; (v) determining which patients should undergo immediate coronary angiography on hospital admission; and (vi) clarifying the importance of extracorporeal membrane oxygenation during CPR.

Keywords: acute cardiac care, automated external defibrillators, cardiopulmonary resuscitation (CPR), intensive care medicine, sudden death, out-of-hospital cardiac arrest.

Background

Cardiac disease is the most common cause of mortality in the western world, and the majority of cardiac deaths are due to out-of-hospital cardiac arrest (OHCA) [1]. In Sweden, there are an estimated 5000–10 000 OHCA each year [2], which represents a major public health problem. Reported survival rates after OHCA vary considerably. This is in part related to the type of cardiac arrest studied. The majority of studies have investigated OHCA only from cardiac causes, some have included all types of OHCA whilst

others have only considered witnessed OHCA and/or those with ventricular fibrillation (VF) as the first registered rhythm. In general, overall survival from OHCA is low with about 5–10% of patients surviving, with the exception of a few controlled settings (e.g. in casinos, airports and some cities) [3, 4]. Previous investigations have shown that a majority of patients with OHCA do have symptoms prior to the arrest [5, 6]. The most common symptoms are angina pectoris, dyspnoea, nausea/vomiting and dizziness or syncope. These are very similar to the symptoms of acute myocardial infarction, the most common cause of

cardiac arrest. Sudden cardiac death was found to be the first manifestation of heart disease amongst 40–60% of all patients in population-based studies from Maastricht, the Netherlands [6] and Framingham, MA, USA [7]. Similar data have been reported from the UK [8].

The mechanisms underlying cardiac arrest are numerous and can be divided into cardiac and noncardiac causes (Tables 1 and 2). Establishing the aetiology of the condition is difficult. Because the vast majority of OHCA patients die outside hospital or in an emergency department, many do not undergo an autopsy; and in a large proportion of cases, there is a lack of information about comorbidities and medication.

Despite increased emphasis on both primary and secondary prevention (and particularly implantable cardioverter defibrillator, ICD, usage in the latter), in the majority of patients it is not possible to predict an OHCA prior to the event. This is demonstrated by incidence and prevalence data reported by Myerburg *et al.* (Fig. 1). As demonstrated in this figure, current ICD recommendations [9] apply for those patients with the highest incidence rates. However, these patients only comprise a small proportion of the total number of patients with OHCA. Thus, at present, the vast majority of patients are still dependent on cardiopulmonary resuscitation (CPR).

Time intervals from cardiac arrest to start of CPR and defibrillation have increased in Sweden [2, 10]. Also, the proportion of patients found in VF on arrival of the ambulance has declined [10–12]. Survival, on the other hand, has remained unchanged [11] or even increased [10, 12], with the largest increase seen during the last decade.

Table 1 Cardiac causes of cardiac arrest

Ischaemic cardiac disease (coronary artery disease)
Ischaemic cardiomyopathy
Dilated cardiomyopathy
Hypertrophic cardiomyopathy
Non-atherosclerotic disease of coronary arteries
Valvular heart disease
Arrhythmogenic right ventricular cardiomyopathy
Infiltrative and inflammatory myocardial disease
Congenital heart disease
Primary cardiac electrical abnormalities

Table 2 Noncardiac causes of cardiac arrest

Pulmonary embolism
Lung disease (hypoxic cause of cardiac arrest)
Electrolyte abnormalities
Bleeding, nontraumatic (hypovolaemic cause of cardiac arrest)
Subarachnoid haemorrhage
Drug overdose
Suffocation
Drowning
Sudden infant death syndrome

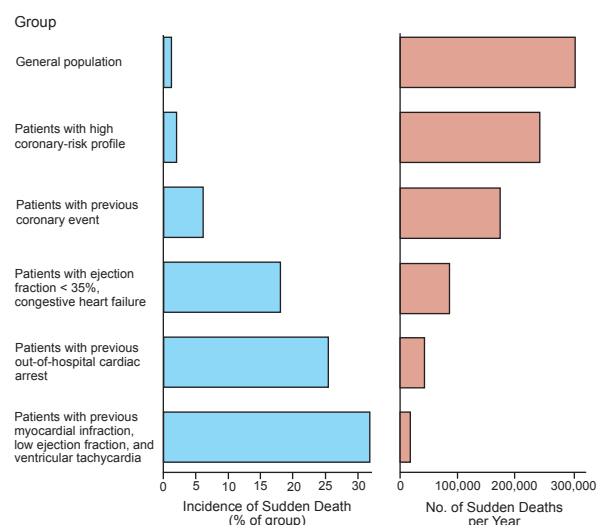


Fig. 1 Incidence and number of sudden deaths in different at-risk patient groups. Adapted from Sudden Cardiac Death. Myerburg *et al.* *Circulation* 1992; 85: 1-2-1-10.

The increase in survival has been particularly marked amongst patients found with a shockable rhythm, and our own studies have shown it is associated with an increase in the proportion of crew-witnessed cases and, to a lesser degree, an increase in bystander CPR [10].

Resuscitation of the OHCA patient is based on the 'chain-of-survival' concept [13] comprising four stages: early access, early CPR, early defibrillation and early advanced cardiac life support. During the last few years, patient management during the in-hospital phase has been increasingly debated and has become important, which has led to the establishment of an additional fifth link in the chain-of-survival model in the form of postresuscitation care.

Here, we will review the progress in research into and treatment of OHCA during the last decade and consider the major obstacles still to be overcome and the future possibilities.

Progress during the last 10 years

Prior to the last decade, the vast majority of cardiac arrest studies were retrospective, and relatively small. However, of note, since then an increasing number of randomized reports have been published.

Early access: agonal breathing, prevention and telephone CPR

In the first link of the chain-of-survival concept (early access), three areas have been shown to be most significant. First, the importance on agonal breathing during the first minutes of cardiac arrest should be stressed. It has been demonstrated that both lay rescuers and healthcare professionals have difficulty in determining the presence or absence of adequate or normal breathing in unresponsive victims [14, 15]. This is most probably because of the presence of agonal breathing, which occurs in around 40% of cardiac arrest patients [16, 17]. As a consequence, delays in recognition of the cardiac arrest lead to delays in calling the emergency dispatch centre as well as in initiating CPR and defibrillation. Teaching emergency dispatchers to understand and recognize bystander descriptions of agonal respiration in patients with OHCA has resulted in a significant increase in offers of telephone-guided CPR in these situations [18]. Secondly, the importance of early access in the context of CPR guidance by telephone from dispatchers to bystanders has become increasingly more recognized during the last decade [18, 19]. Data indicate that telephone-guided CPR increases survival [20]. Thirdly, the use of 'track and trigger systems' to detect deterioration of condition in patients and enable treatment to prevent in-hospital cardiac arrest has become more recognized during the last decade. The results of a meta-analysis demonstrated that medical emergency/rapid response teams and RRT/MET systems were associated with a reduction in rates of in-hospital cardiac arrest [outside the intensive care unit (ICU)]. However, this analysis did not demonstrate lower hospital mortality rates [21]. Nonetheless, recent guidelines recommend a clear strategy for hospitals for the prevention of in-hospital cardiac arrest [22].

Bystander CPR contribution and different CPR techniques

The effects of early CPR on survival have been demonstrated repeatedly. Early CPR doubles or even triples survival after OHCA [23–25]. Furthermore, studies show that bystander CPR prior to ambulance arrival improves survival rates in patients with prehospital VF [26, 27].

The proportion of patients receiving bystander CPR has been increasing in Sweden in the last decade [28]. Since 2000, there has been a marked increase in bystander CPR in OHCA, performed by lay persons. Bystander CPR is clearly associated with positive effects on survival.

The CPR protocol has also been slightly modified over time, and the ventilation/compression ratio changed from two ventilations/15 compressions to two ventilations/30 compressions in 2005 [29, 30]. This ratio remained unchanged in the recently published CPR guidelines; however, the importance of good chest compressions and minimal 'hands-off time' was highlighted [22].

Probably, one of the most important and debated issues during the last decade has been the potential use of compression-only CPR as an alternative to standard CPR in OHCA (i.e. the presence or withdrawal of ventilation). Initially, the results of a single animal study suggested that compression only could be a valid alternative to standard CPR [31]. Furthermore, these findings were confirmed in a prospective but small randomized clinical study [32], as well as in two large population-based observational register studies in which no significant differences were observed in 1-month survival amongst patients with OHCA with either standard CPR or chest compressions only [33, 34]. Following this, in 2010, two large prospective randomized studies showed no significant difference with respect to survival between instructions given by emergency medical dispatchers for compression-only CPR and instructions for standard CPR in patients with witnessed OHCA [35, 36]. As a consequence, new guidelines recommend telephone-guided chest compression-only CPR for untrained rescuers [22]. However, trained rescuers are still advised to give standard CPR with both compressions and ventilation. Nonetheless, some centres (predominately in the USA) have changed their prehospital protocol to an approach that includes 6 min of uninterrupted chest compressions with rhythm analysis and shocks if

necessary with the delay of ventilation and intubation for trained rescuers [37]. These studies have provided promising survival data; however, to date, this new approach has not been shown in a randomized study to be superior to the present protocol.

Another frequently debated issue has been the use of mechanically aided chest compressions following the development of new devices for this purpose. Whilst the results of a few case reports [38] and animal studies [39] have indicated positive outcomes with these devices, two smaller randomized trials using two different devices have revealed unchanged [40] or even somewhat worsened [41] survival rates compared with manual CPR. Presently, the results of two large prospective randomized trials of the Autopulse (CIRC study) and the LUCAS systems (LINC study) are awaited. Positive survival data and clear implementation strategies are needed before these devices can be recommended on a large scale.

First responders and automated defibrillator programmes

With the development of self-instructing automated defibrillators (AEDs), the concept of defibrillation beyond conventional emergency medical service (EMS) and ambulance crews to nonmedically trained personnel is spreading rapidly and is sometimes generalized within the concept of public access defibrillation (PAD). Three types of groups can be identified: (i) untrained lay rescuers using PAD; (ii) trained lay persons using PAD; and (iii) first responders via (theoretically) simultaneous paired dispatches from central dispatch centres.

First, a few studies have investigated the use of PAD by untrained lay rescuers, with promising survival results. Whitfield *et al.* presented data regarding the use of 681 AEDs, which were located in 110 public places (for use by volunteer lay first responders). They showed that VF was the first recorded rhythm in 82% of 146 cases and that 25% of 177 patients with witnessed OHCA survived to hospital discharge [42].

Secondly, a few studies have demonstrated impressive survival data with the use of trained lay rescuers using AEDs. In the PAD Trial, the Public Access Defibrillation Trial [43], training and equipping volunteers to attempt early defibrillation within a structured response system could increase survival after OHCA in public locations

(30 survivors in the intervention group versus 15 survivors in the control locations). The authors concluded that trained lay persons can use AEDs safely and effectively. However, the number of lives saved in this study was small in relation to the number of centres included (19 000 volunteer responders from 993 community units). Valenzuela and colleagues demonstrated that rapid defibrillation by nonmedical personnel using AEDs in casinos can improve survival after VF OHCA [44]. In this study, survival data were extremely impressive with an overall survival rate of 53% and a surprisingly high survival rate of 74% for those who first received defibrillation no later than 3 min after a witnessed collapse. Page *et al.* [45] demonstrated the efficacy of the use of AEDs aboard commercial aircrafts, with 40% of patients being discharged from hospital after conversion of VF.

Thirdly, most studies, however, have used first responders for intervention [46–52]. First responder programmes have varied in terms of intervention (police, fire departments or both), type of control (historical controls or concurrent EMS) and cardiac arrest population (all cardiac arrests, witnessed only, VF cardiac arrests or only cardiac causes). Therefore, this makes comparisons between studies somewhat difficult. Nonetheless, we conclude that dual dispatch PAD programmes overall tend to decrease the time interval from collapse to CPR and defibrillation, and increase survival (predominately for witnessed or VF OHCA patients).

Hospital care

Historically, few studies have focused on in-hospital mortality after OHCA, and a direct effect on survival of in-hospital factors has been demonstrated by only a few of these. However, during the last few years, greater attention has been directed towards the postresuscitation phase of OHCA. This fifth phase in the chain-of-survival concept addresses different aspects of the treatment of the successfully resuscitated patient. Within this phase, three major areas should be highlighted: (i) ‘mild therapeutic hypothermia’; (ii) in-hospital and particularly ICU care; and (iii) coronary angiography including percutaneous coronary intervention (PCI).

First, the use of cooling in cardiac arrest is often known as mild therapeutic hypothermia. Following the report of data from two (rather small) investigations showing improved neurological outcome in

comatose survivors after VF with therapeutic mild hypothermia [53, 54], this treatment has become widely implemented in clinical practice. Mild therapeutic hypothermia is further discussed below.

Secondly, treatment and factors relating to survival during hospitalization, and predominantly ICU care, have received increasingly more attention in the last 10 years. In-hospital factors found to be associated with (poor) survival are high body temperature, elevation of blood glucose, acidosis, seizures, old age, a long delay before sustained return of spontaneous circulation, elevated potassium concentration and use of low concentrations of beta-blocking agents [55, 56]. It has been suggested that therapeutic options can be divided into four groups [57]: (i) optimization of physiological status (body temperature, blood pressure, blood glucose, acid-base balance and electrolytes); (ii) revascularization (thrombolysis, PCI and coronary artery bypass graft); (iii) antiarrhythmic therapy (ICD, beta-blocking agents and amiodarone); and (iv) anticonvulsant therapy.

A Norwegian group have proposed a standardized treatment protocol for the first few days in the ICU for patients who have been successfully resuscitated [58]. This protocol comprises reperfusion and maintenance of blood pressure (mean arterial pressure >65–70 mmHg), central venous pressure (8–12 mmHg), external chest compression, ECC rate (60–100 min⁻¹), temperature (33 °C for 24 h), ventilation (saturation of O₂ in blood 95–98% and partial pressure of CO₂ 5–6 kPa) and blood glucose (5–8 mmol L⁻¹). In an observational study (comparisons with historical controls), the introduction of this standardized treatment protocol led to improvements in hospital discharge rate, neurological outcome and 1-year survival. Based on a multivariate logistic analysis, hospital treatment in the intervention period was the most important independent predictor of survival. However, a randomized controlled study is still necessary to confirm the Norwegian data.

Thirdly, the increased and widespread use of coronary angiography including PCI during the last decade should be highlighted. Over the last few years, it has been well recognized that postcardiac arrest patients with ST-segment elevation myocardial infarction (STEMI) should undergo early coronary angiography and PCI [22]. Also, because chest pain and/or ST elevation are rather poor predictors of acute coronary occlusion in these patients,

current guidelines specify that this intervention should be considered in all postcardiac arrest patients who are suspected of having coronary artery disease. However, it should be noted that the contribution of early revascularization to survival is unknown, and the need for a prospective randomized study in this patient group is essential.

The Stockholm experience

Until recently, the OHCA survival rate in the larger Stockholm area was low, that is, 2–3% [59]. Retrospective analyses showed that the most probable reason for this low survival rate was a relatively long time for arrival of the rescue team (6–8 min), partially due to a low density of ambulances in the area. At that time, the medical rescue team consisted only of ambulances equipped with defibrillators. To increase the availability of rescue resources, we in 2005 initiated a project including the Stockholm fire brigade within the rescue team [60]. By equipping members of the fire brigade with AEDs and including them in the rescue team, alarmed by the dispatch centre, we were able to shorten the time to arrival. Similarly, survival was improved compared to historical data [52]. As a next step, we also included the Stockholm Police Force in the same manner, further improving the outcome.

Figure 2 shows the survival rate after OHCA in Stockholm during the last 10 years. Since late 2005, the fire department has been integrated in the dispatch protocol for OHCA in the wider Stockholm area. In parallel with administrative changes in the dispatch routines, we also started to promote the use of AEDs in public places and to encourage CPR by first responders. To date, more than 125 public AEDs are available mostly in areas

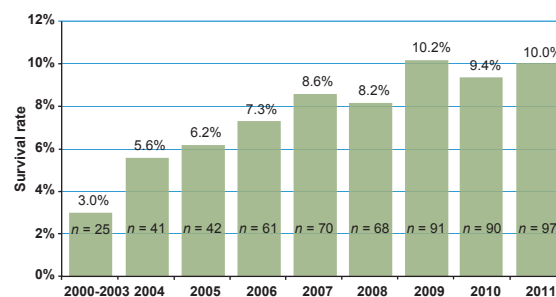


Fig. 2 Change in time of survival rate after out-of-hospital cardiac arrest in Stockholm.

with a high population density. We are currently analysing the number of verified situations in which an AED within the project has been used for defibrillation and survival in these cases.

First responder CPR has been encouraged by offering telephone instructions from the medical dispatch centre. Approximately nine of 10 witnesses agree to start CPR after receiving instructions from the dispatch centre [16]. The likelihood of providing first responder good-quality CPR can be improved as it has recently been shown convincingly that a simplified CPR technique using compression only is at least as good as standard CPR including ventilation [35, 36, 61]. See below for further discussion of chest compression only.

Future problems and possibilities

During the last 10 years, advances have been made in the field of OHCA research and treatment. As already mentioned, survival in our own region has been dramatically improved in the last few years. Nevertheless, about 90% of patients still die after an OHCA, leaving much scope for improvement. We believe that much of this improvement may come from increased focus during the next 10 years on a number of key areas: identification of high-risk patients, increased use of bystander CPR and AEDs, cooling techniques, the use of chest compression only and extracorporeal membrane oxygenation (ECMO).

Identification of high-risk patients: early warning symptoms and genes

Currently, only patients with the highest risk of OHCA, that is, a small proportion of the total number, can be identified. This has been repeatedly demonstrated, and thus, the vast majority of patients are still dependent on CPR. Hopefully, research will enable more at-risk patients to be identified prior to cardiac arrest. In this context, genetic screening may be important. The initial results of familial aggregation studies have suggested that genetic factors may confer susceptibility to OHCA in the general population [62]. The potential contribution of environmental factors as determinants of OHCA is another field of interest. Although this area has been gaining interest from different research groups, few studies have been reported to date. The majority of OHCA patients experience symptoms prior to their arrest [5, 6]. These patients need to reach professional help

sooner than at present. Earlier treatment would lead to both fewer cases of OHCA and to earlier CPR for those needing it. Therefore, new methods need to be established to recruit life savers. In Stockholm, we are currently evaluating a concept whereby mobile phone technology can be used to identify and recruit nearby CPR-trained citizens for bystander CPR during an OHCA prior to the arrival of an ambulance [63]. Preliminary data indicate that this mobile phone technology can indeed be used to identify and recruit nearby CPR-trained citizens in a large proportion of cases.

Increased use of bystander CPR

Schools

Most OHCA occur at home, and such events are associated with poorer prognosis compared with arrests that take place in a public area. This is probably in part due to a knowledge gap amongst a large proportion of the population about how to perform CPR. Educating all schoolchildren in CPR on a national basis might be a way not only to increase the proportion of patients receiving bystander CPR but also perhaps to increase the quality of CPR. In most countries, such education in CPR is not mandatory. Learning CPR should in the future be a high priority too. In Sweden, after much debate for many years, teaching first aid including CPR became part of the national primary school curriculum from 2010 [64]. However, the long-term effects of CPR education for schoolchildren on bystander CPR rates and survival have yet to be determined. This issue was addressed in a Danish study conducted in 2005 in primary schools [65]. In this study, 35 000 manikins (Mini-Anne) were distributed to 806 primary schools. A 24-min instructional DVD was used to teach CPR, and children were encouraged to pass on their knowledge to family members and friends. This educational strategy seemed to be effective with 2.5 extra persons trained per pupil. However, the incidence of bystander CPR in the months after the project did not increase significantly compared to the previous year (25% vs. 27.9%; $P = 0.16$). This raises questions with regard to CPR education in schools. Should the same type of education be used in schoolchildren as in adults? And what type of education is most appropriate/effective? Surprisingly, few studies have addressed these questions. The same Danish research group also evaluated skill retention at 3 months using the same educational method as described above in schoolchildren and compared the findings with

those from adults recruited from an insurance company. Three months after a CPR course, adults had higher overall BLS skills than children when using this educational method [66]. However, children were better able to perform CPR with less 'hands-off time'.

Simplified techniques

The traditional and simple cardiac massage to deliver circulation to the brain and body was proposed in a seminal paper by Kouwenhoven *et al.* [67]. Is it possible that over the years this simple method has been made too difficult for lay bystanders by the introduction of ventilation? We know from recent studies that bystanders, regardless of whether they are untrained or trained, laypersons or medically trained personnel hesitate to perform mouth-to-mouth ventilation [68]. The two major reasons are clear; it is too difficult for lay persons to perform mouth-to-mouth CPR and/or bystanders seem to be afraid of exposure to transmitted diseases. Ornato *et al.* [69] found that amongst BLS instructors in Virginia, USA, 40% of those who had performed CPR during previous 3 years reported hesitating to provide mouth-to-mouth CPR due to fear of exposure to diseases. Similarly, amongst medical staff working at a university hospital, only 45% would perform mouth-to-mouth CPR on an unknown patient and only 16% would do so on patients with blood on their lips [68].

Increased use of AEDs

The spread of AEDs in public places to nonmedical persons is rapidly increasing. The latest AEDs are becoming smaller, less expensive and easier to use. This is obviously important as early defibrillation is perhaps the most important link in the chain-of-survival concept. However, it is unclear exactly where these AEDs should be placed. Guidelines provide very few and vague recommendations [22], all of which are based on relatively old and diverse retrospective studies. Better identification of high-incidence sites is required to know where to place these devices. Also, we have noted in our own studies that many AEDs in public places are not used due to lack of knowledge of their whereabouts. One way of preventing this in future would be the placement of AED locations on emergency dispatch maps, which could enable dispatch centres to inform the caller of the nearest location of an AED. In addition, mobile positioning systems could be used with SMS recruitment of volunteers

equipped with AEDs to reach patients prior to usual emergency personnel [63]. In some countries, there is legislation requiring AEDs to be placed in public buildings and areas. However, there are large variations in requirements between different countries.

Hypothermia: when, where, how and in which patient population

The use of mild therapeutic hypothermia in cardiac arrest has been recommended and widely used following the publication of the results of two small randomized clinical trials in 2002 [53, 54]. The results of these studies demonstrated improvement in neurologically intact survival for comatose cardiac arrest patients admitted to hospital with either VF or ventricular tachycardia. These findings have led to the worldwide implementation of cooling after cardiac arrest but have to some extent become criticized in relation to the rather small number of patients included in the studies [70]. Thus, somewhat surprisingly, current CPR guidelines now suggest cooling to be considered even if the presenting rhythm is not VF or VT. This recommendation is debated [22]; even if mild hypothermia is a promising treatment after a cardiac arrest, there are still a number of unanswered questions. What is the optimal temperature? When should treatment be started? What type of cooling method should be used? And which patients are likely to benefit?

An ongoing Scandinavian study is investigating the optimum target temperature in the ICU setting [71]. Furthermore, proponents of cooling after cardiac arrest have performed prehospital studies. As in many other acute situations (acute myocardial infarction or stroke), it is believed that 'the earlier the better'. Several smaller trials have clearly demonstrated that prehospital cooling can be carried out safely and with a high degree of efficacy. Different methods have been used. Examples include surface cooling using ice packs (target temperature achieved in 7.5 h) [72], a cooling cap (target temperature achieved within 6 h) [73] and Ringer acetate solution (used in a Finnish study to demonstrate reduction in temperature from 35.8 °C in a prehospital setting to 34.0 °C upon hospital arrival) [74]. Using a new intra-nasal method of intra-arrest cooling (i.e. cooling during cardiac arrest), it was shown that time to target temperature could be achieved 2 h earlier than in patients cooled upon arrival to hospital [75]. However, not all prehospital studies have been positive. In a randomized study conducted in

Australia, use of early cooling did not demonstrate any survival benefits [76]. In this trial, all patients received cold Ringer acetate solution administered as a bolus of 10 mL kg⁻¹ followed by infusion of 100 mL min⁻¹ up to a target of 2000 mL, and cooling before hospital admission was compared with cooling after arrival. However, the study investigators could not reach the somewhat unusual primary end-point of 'functional status at hospital discharge' (48% prehospital cooled and 53% hospital cooled; ns).

Is chest compressions only a suitable method of CPR?

Optimal CPR, providing adequate cerebral circulation, traditionally includes a combination of both chest compressions and ventilation. However, it is well known that adequate artificial ventilation may be difficult to achieve in OHCA. Based on animal studies, it has therefore been suggested that compression-only CPR might be sufficient to provide an adequate oxygen tension in the blood. Compression only would also be easier to perform for a first responder without previous training. Additionally, avoiding physical ventilation could possibly, for hygiene reasons, make CPR more attractive.

Rationale behind chest compressions only

Coronary pulse pressure (CPP) is the pressure needed to perfuse the heart muscle. The CPP is the left ventricular end diastolic pressure minus the diastolic pressure in the right atrium. Under normal physiological conditions, this pressure is about 60 mmHg. During a cardiac arrest, the pressure falls to 0 mmHg, and it has been suggested that CPP needs to be at least 15 mmHg to achieve return of spontaneous circulation [77, 78]. As seen in Fig. 3, interruption of chest compression results in a markedly lower CPP in terms of blood flow during CPR. Furthermore, an increased frequency of positive pressure ventilation may reduce survival rate due to interruption of chest compression [79] but also due to obstruction of venous return to the central circulation as a result of the increased and thereby higher intra-thoracic pressure during the ventilation phase of CPR [80]. These important issues probably provide indirect proof of the importance of (uninterrupted) chest compressions.

Historically, only observational register and animal studies have supported one or other of these strategies as the best method to perform CPR. However, several recent studies have tested the effectiveness of chest compressions only using

-The blue-dashed line represents the minimum CPP required to carry oxygenated blood to the brain and heart.

-The black-spiked line represents chest compressions performed, with pauses to put two breaths in and re-oxygenate the blood.

-The red-solid line represents the CPP generated by the chest compressions.

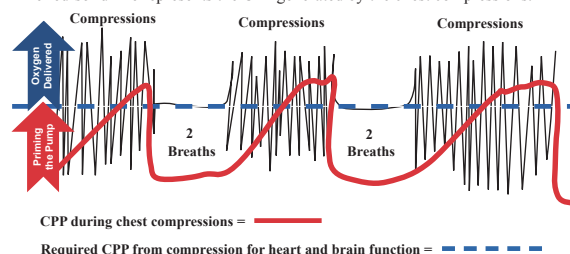


Fig. 3 Coronary pulse pressure (CPP) during cardiac arrest. From Kern and Berg *et al.* *Resuscitation* 1998 and *Circulation* 2001.

both register-based and prospective randomized trials in OHCA populations [33–36]. The general outcome of these studies is that compression only seems to be at least as effective as standard CPR in terms of mortality.

The results of a meta-analysis of three prospective studies demonstrated that compression only is associated with improved survival, compared with standard treatment [61]. The main argument against implementing compression only as a standard CPR technique is that the results presented are based on lay persons having received instructions on CPR from a medical dispatch centre. It can thus still be argued that high-quality standard CPR performed by trained lay persons or medical personnel is superior to compression only.

Thus, present guidelines still recommend ventilation as part of the CPR procedure for trained personnel. In situations in which CPR is performed by nonmedical personnel with or without telephone instructions, compression only is accepted as standard treatment [22].

Thus, there is still a need for a randomized trial not only amongst bystanders but also amongst EMS and hospital personnel to determine which CPR method will be the 'drug of choice'.

Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation is an extracorporeal technique that provides cardiac circulation and blood oxygenation and is well established

for several conditions involving circulatory and/or respiratory shock. However, only few studies have investigated its use in the cardiac arrest setting. International data indicate that the use of extracorporeal CPR [using extracorporeal life support (ECLS); ECMO-CPR] is increasing. CPR using ECLS was assigned a low-level recommendation in resuscitation guidelines for in-hospital cardiac arrest patients in 2005 [81].

Most studies of ECMO for cardiac arrest patients have been conducted in hospital. The majority of these few studies used retrospective cases from single-centre databases. Almost all studies had refractory cardiac arrest as an inclusion criterion and included patients between 15 and 80 years of age. In general, these studies presented impressive survival data; patients included were those with the 'worst' prognosis with refractory cardiac arrest (i.e. not responding to standard CPR) and, still, the survival rate was around 30%.

The two most notable studies are those by Chen *et al.* from Taiwan [82] and Shin *et al.* from Korea [83]. Chen *et al.* conducted a prospective observational study on the use of ECMO-CPR for patients aged 18–75 years with witnessed in-hospital cardiac arrest of cardiac origin undergoing CPR for more than 10 min, compared with patients receiving conventional CPR. Matching was based on propensity score to ensure that potential prognostic factors did not differ in the two groups. The results from this study showed that extracorporeal CPR had short-term and long-term survival benefits compared with conventional CPR in patients with in-hospital cardiac arrest of cardiac origin. Shin *et al.* retrospectively analysed data from 406 patients with witnessed in-hospital cardiac arrest receiving CPR for >10 min (of whom 85 underwent ECLS) using almost identical inclusion criteria as in the study from Taiwan. Data from this trial showed a survival benefit of ECMO-CPR compared with conventional CPR in patients who received CPR for more than 10 min.

Data from clinical studies to investigate the use of ECMO in OHCA are lacking, and therefore, this method must be recognized as experimental outside hospital at present. A few case reports of the use of ECMO-CPR prehospital admission have been published (mostly showing negative effects on survival) as well as a few case series, but at present, there are no robust data to support the use of ECMO-CPR in a prehospital setting.

In summary, ECMO-CPR appears to be a promising tool especially in patients with in-hospital cardiac arrest. However, there are still many limitations that need to be addressed. First, most reported studies have been single centre, nonrandomized and retrospective. Thus, inclusion and intervention bias and the Hawthorne effect are probably not insignificant. Secondly, resuscitation details (i.e. time from cardiac arrest to start of CPR or defibrillation) are largely unknown. Third, the combination of ECMO-CPR and hypothermia has been largely unstudied. Fourthly, the quality of CPR in these situations has not been reported. And finally, cannulation techniques and times require more investigation. Nevertheless, we believe that ECMO-CPR is one of the most promising treatments for cardiac arrest patients. Future studies will clarify its exact role in the chain of survival.

Summary

Out-of-hospital cardiac arrest is a major public health problem. During the last decade, much progress has been made in research and treatment. The importance of early access, recognition of agonal breathing and telephone-guided CPR has been highlighted. The use of telephone-guided compression-only CPR by bystanders as an alternative to standard CPR in OHCA is now recommended for untrained rescuers. PAD with AEDs is rapidly spreading, especially for dispatched rescuers. Postresuscitation, use of therapeutic hypothermia, the importance of specific prognostic survival factors in the ICU and the widespread use of percutaneous coronary intervention have all been investigated.

Nevertheless, most patients still do not survive an OHCA. Further studies are needed to simplify CPR techniques, identify high-risk patients prior to arrest, recruit AEDs in PAD, increase understanding of the use of therapeutic hypothermia and determine the importance of ECMO during CPR.

Conflict of interest statement

No conflicts of interest to declare.

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