

Has survival after out-of-hospital cardiac arrest improved during the last 50 years?

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ABSTRACT:

In the last fifty years many new interventions and techniques have improved the survival for victims of out-of-hospital cardiac arrest, but the reported overall survival rates have not increased accordingly. In this paper, which is a condensed version of my trial lecture presented 13th June 2007, I identify five milestones that should have improved survival; basic cardiopulmonary resuscitation (CPR), lay persons' CPR, external defibrillation, international collaboration to standardize training and performance in CPR, and systematic postresuscitation care including therapeutic hypothermia. The demographic changes and delays in implementation of knowledge into clinical practice might be reasons for unimpressive changes in survival over these years. The reappraisal of good quality basic CPR by bystanders and professionals is probably the easiest and most inexpensive means to improve survival in the near future.

KEYWORDS: Cardiac arrest, Survival, Review, History

Introduction

During the last 50 years much has changed in the way we practice medicine and this includes our approach to sudden deaths outside the hospital. In this review, I will try to evaluate the changes that stand out as milestones in the treatment of cardiac arrest, but also discuss the difficulties of reviewing survival rates over the time span mentioned. There are several excellent reviews regarding the historic development of cardiopulmonary resuscitation (CPR) and I refer the interested reader to these ¹⁻⁶.

The survival rates after cardiac arrest 50 years ago were ignorable, unless it occurred during anesthesia and surgery. Since the introduction of Chloroform anesthesia in the late nineteenth century various cardiodepressive anesthetic agents had given ample opportunities to practice open chest cardiac massage and also direct defibrillation of the heart ^{7,8}. Outside the hospital only resuscitation after drowning was attempted, but the survivors might not have been in full cardiac arrest as we understand it today. Today the incidence of sudden, unexpected out-of-hospital cardiac arrest where CPR is attempted of around 50/100 000 per year, and most major EMS systems report survival rates in the range 1-10% for all out-of-hospital cardiac arrests ⁹. And even if the age distribution of these victims preclude the return to "tax-payer" status, more than 90% of the survivors have acceptable neurological function and the survivors can expect to live as long as those at the same age with acute myocardial infarction without cardiac arrest ¹⁰⁻¹².

How to compare survival rates

It is hard to evaluate the success-rates from the early publications. Apparently, the survival after cardiac arrest in Oslo if bystander CPR was initiated during the late 60-ies was 36%, and in Belfast it was 31% among all patients with cardiac arrest outside the hospital ^{13,14}. Two problems are obvious:

1. Unknown nominator, i.e. what is the definition of a survivor.
2. Unknown denominator, i.e. what is the definition of the group of patients with cardiac arrest.

Some of the possibilities are shown in Figure 1. One of the major scientific breakthroughs has been the Utstein-papers that state common definitions of these groups ^{15,16}. The most honest report would be to count survivors among all patients

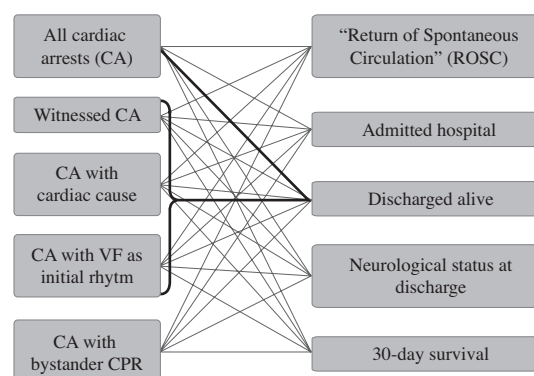


Figure 1. The figure shows some of the possible mixes of nominators (patient outcome) and denominators (number of patients) that have been reported in the literature. The heavy connections represent the outcome measures most often reported.

with cardiac arrest, but cessation of cardiac function is a part of all deaths; sudden, natural, and after prolonged intensive care. The denominator will therefore be influenced by local and cultural variations in which patients that are included, and protocols to withhold treatment in case of obvious death. Many consider the subgroup of patients with presumed cardiac cause of the arrest and VF as initial rhythm to be a more uniform sample, and this group is often used to benchmark the emergency services.

Secondly, the population changes as the demographical profile changes. In Norway, as in most industrialized countries, the general population is aging. As a result, more people live with chronic diseases. On the other hand, treatment for atherosclerotic disease has become much more efficient. Treatment of myocardial infarctions has also changed a lot with acute coronary interventions and secondary prophylaxis with beta-blockade to prevent arrhythmias and aggressive treatment for hypercholesterolemia and anti-coagulation. These changes have been speculated to cause the decline in patients with VF as the initial rhythm and would tend to increase the proportion of patients with very sick hearts and hence poor prognosis^{17,18}.

Milestones in the treatment of cardiac arrest outside the hospital

Each decade (roughly) has its milestone and I will discuss them in the context of the chain of survival first published in 1991 and amended in 2005^{19,20}. The milestones in the treatment of out-of-hospital cardiac arrest the last 50 years can be summarized by the following:

1. The (re-)introduction of external chest compressions.
2. Expanding this opportunity to the out-of-hospital environment and to lay people.
3. The external defibrillator and the semi-automatic defibrillator
4. The international collaborations to collect systematically the knowledge about treatment of cardiac arrest.
5. Therapeutic hypothermia and systematic post-resuscitation treatment.

First link: early recognition and activation of the emergency system

In all published reports, the survival differs markedly between witnessed and unwitnessed arrests. The Swedish registry of out-of-hospital cardiac arrests currently has more than 40 000 events included, and in the annual reports, this relationship is firmly established in large groups of patients²¹. Already in the first report of a physician-manned ambulance in Belfast, Pantridge speculates that one important factor for the increased survival was the reduced patient delay from the first symptoms to contact with the emergency services¹⁴. In the 70-ies one emergency telephone number was established and promoted in Seattle, and this concept has been adopted in many countries²². Although information campaigns about the emergency telephone number and which symptoms that

should initiate contact have not been demonstrated to affect survival, the effect is incremental and studies will easily be underpowered in populations where this number is already partially known^{23,24}.

The effect of early recognition and alarm can thus only be evaluated retrospectively, with all the limitations of having the bystanders recall time-points in a very stressful situation. However, data from the Swedish registry have shown higher survival to be associated with shorter delays, even after correction for other factors in a regression model²¹. The longitudinal data from the same registry show a steady decline in this delay, but I think all of us working in the pre-hospital environment see the potential for improvement here; all too often we hear that bystanders in face of alarming symptoms, call their doctor nephew or hesitate because of fear that the incident is not serious enough instead of immediately activate the emergency services.

I will not go into details about organization of the call centers for such emergency calls or the dispatch systems. Suffice it to say that there are certainly ways to optimize these links in the chain of survival as well.

The second link: early cardiopulmonary resuscitation

Whether this is done by bystanders or by professionals, the importance of these simple steps has been solidly demonstrated. The combination of the simple maneuvers of opening of the airways, expired air positive-pressure ventilation, and external chest compressions will always be connected to the names of Peter Safar, William Kouwenhoven, James Jude, and James Elam²⁵⁻²⁸. To combine these maneuvers in the treatment of sudden cardiac arrest, and to recognize the simplicity that allowed this to be taught and used by anyone anywhere is certainly one of the milestones in the treatment of cardiac arrest (Table 1). The role of the toy manufacturer, Åsmund Lærdal in close cooperation with the anaesthesiologist Bjørn Lind, both living in Stavanger, Norway, was to make it possible to train many people and lay people with the introduction of the first manikins for training mouth-mouth-ventilation in 1960 and chest compressions in 1969⁵.

Table 1

“Anyone, anywhere, can now initiate cardiac resuscitative procedures. All that is needed are two hands.”

W.B. Kouwenhoven²⁶

The introduction of these techniques to lay people was not endorsed by the AHA until 1974 due to concerns about hygienic and aesthetic issues and fear that the techniques could cause harm. In their landmark paper from 1976, Lund and Skulberg reported that resuscitation had been started in 12% of the cases of out-hospital cardiac arrest, and the effect

on survival was impressive; 36% versus 8% in those patients where CPR was not started until the arrival of the ambulance¹³. The first large study of massive educational efforts among lay people was performed in Seattle and during the late 70-ies more than 200 000 citizens were taught CPR, the proportion of patients receiving bystander CPR increased from 5 to 34% and among those who received bystander CPR there was a doubling in survival²⁹. It is interesting to note, that the Swedish cardiac arrest registry finds the same doubling in survival rates in patients with bystander CPR regardless of ambulance response time³⁰. One of the possible reasons for improved survival in the group that received bystander CPR is increased proportion of patients still in VF at ambulance arrival.

This was also the possible explanation in three studies attempting to classify the quality of Bystander CPR based on palpable pulsations in the femoral artery and visible chest rise. These studies found improved survival not only in the group that received bystander CPR, but an even higher survival in the group that received good quality bystander CPR³¹⁻³³. However, such quality was only found in a minority of the cases. The fact that good quality is better than poor quality is in excellent agreement with all animal studies that have been performed. The problem, even in an experimental setting, is of course to single out which part of CPR that is the most important and to study one aspect of quality in isolation.

The third link: early defibrillation

Defibrillation is the process of terminating an un-organized electrical activity in the heart. Mostly, this is achieved with a trans-cardial electrical current that depolarizes and leaves most of the cardiomyocytes in a refractory phase simultaneously and then the group of cells with the highest internal pacemaker potential will recover the control of the cardiac rhythm and organized electrical activity will result in cardiac output. From this definition it is obvious that defibrillation will meet with very limited success if the conductive and mechanical properties of the heart are too affected by the underlying pathophysiology to function properly.

For the patient with VF or non-perfusing ventricular tachycardia (VT), defibrillation is a necessary step for survival and the rapid development of transportable and even portable defibrillators in the late 60-ies and early 70-ies, made rapid defibrillation possible. Semi-automatic defibrillators (AED) make even earlier defibrillation possible, as the theoretical knowledge required for the operation of such is very limited³⁴. Biphasic defibrillators have not been shown to increase survival, but are at least as effective as the older defibrillators and they require smaller batteries, enabling smaller and cheaper defibrillators³⁵.

The “world record” in fast defibrillation and high survival is from the casinos in Arizona, where most patients received CPR and shock within 5 minutes based on decentralized AEDs and training of security personnel in both CPR and use of

defibrillators³⁶. Again data from the Swedish registry gives us a nice relation between delay from collapse to defibrillation and survival³⁷. This delay depends on the organization of the emergency medical systems and in Scandinavia the median time to defibrillation has increased in Sweden from 8 to 9 minutes²¹ and remained unchanged around 11 minutes in Oslo (Kjetil Sunde, personal communication). Of course, geographical factors are different from the big cities in the US; Seattle has a median response interval of about 5 minutes and a survival rate for witnessed patients with initial VF of 30-35%¹⁸.

The logical consequence would be to distribute AEDs widely, but even at the O’Hare Airport in Chicago, which is one of the largest airport in the world with more than 80 million people passing every year, they experienced only 20 witnessed cardiac arrests during two years³⁸; equivalent to an incidence of 5 arrests per 100 000 persons per year – that is only 1/10 of the numbers seen in Oslo and most other places. This illustrates the fact that more than 70% of sudden cardiac arrest occur in private homes, and that the sickest people don’t travel by airplane. Even if we are able to make AEDs so cheap that they can be placed everywhere, the success will depend on our ability to educate people about the first to links in the chain; to recognize an arrest, and to start with the simple lifesaving steps of basic CPR.

The fourth link: post resuscitation treatment

This fourth link was previously known as “early advanced treatment”, but the effect of early advanced treatment such as endotracheal intubation and *i.v.* medications have been questioned. The third phase of the OPALS study in Canada found no effect on overall survival with the addition of these steps in a system that already had implemented early defibrillation and systematic responses to cardiac arrests³⁹.

In the recent years, we have seen the re-discovery of the neuro-protective effects of hypothermia after return of spontaneous circulation (ROSC). This is one of the few interventions in cardiac arrest actually proven in randomized trials, so far only confirmed in large studies for patients with witnessed cardiac arrest with VF as initial rhythm that are still unconscious at arrival to the hospital^{40,41}. It also appears that it pays to have a systematic approach to the intensive care treatment in hospital; with simple targeted protocols including therapeutic hypothermia, coronary revascularization if indicated, sedation, blood glucose control, ventilator therapy, and circulation, a doubling in survival among those admitted to hospital have been shown¹².

So, in conclusion, we know what to do in all these links – so why don’t we?

International guidelines

The operations need to be put into a system, to enable training and effective performance in a time of crisis. From the first

standards presented in 1974⁴² to the latest guidelines in 2005¹⁹ the best knowledge has been translated to practicable steps. The change from standards to guidelines reflects an increasing acknowledgement of the unique difficulties encountered in each situation. But have these guidelines in themselves increased survival?

There are no such studies, unfortunately. The closest we can get is a recent publication from Seattle where they took a head start on the new guidelines and implemented a single shock protocol and 2 minutes of CPR between each intervention in 2004. Compared with historical data, the survival among the witnessed cardiac arrests with initial VF increased from 33 to 46%⁴³. If some reported survival rates are plotted along a time axis, we notice no leaps in survival at the times of guideline introductions (Figure 2). The most apparent feature of such a figure is the increasing spread of reported survival rates. This might be a sign of a more mature field of research, where poor performance is equally interesting to report as the enthusiastic reporting of “new world records”.

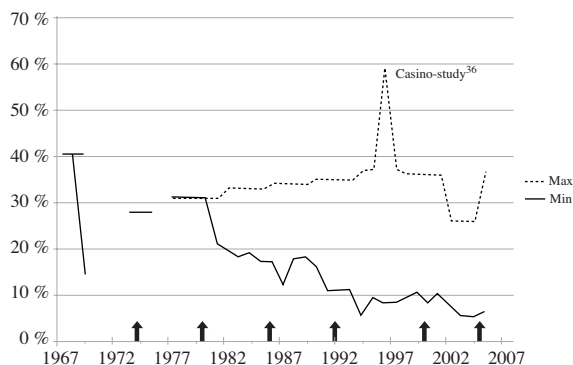


Figure 2. The figure presents some outcome data reported the last 40 years for patients with witnessed cardiac arrest with VF as initial rhythm. Publication of “new” guidelines are marked with arrows. The survival rates are taken from Belfast¹⁴, Göteborg¹⁷, Oslo^{10-13,31}, Arizona³⁶, Canada³¹ and Seattle^{18,22,29,43}.

The formula of survival

The lack of quantum leaps in survival at each new intervention or guideline revision is explained by the delay from scientific finding to change in guidelines and education, and in the delay to implementation of new knowledge into clinical practice. This is the concept of the “formula of survival” – each factor is between 0 and 1 and multiplies into a fraction of theoretical survival (Figure 3)⁴⁴. If we agree that we know quite a lot about the first two factors; scientific knowledge and education, we can also agree that the last factor – implementation – is the next challenge. In fact, the lack of increased survival altogether during these years, might be explained by this delay

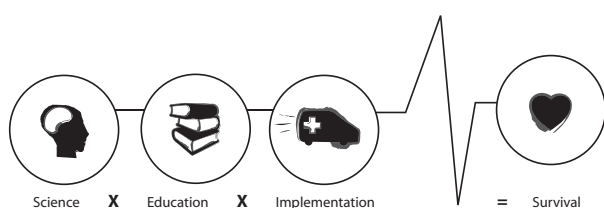


Figure 3. The formula of survival

in implementation. We have barely grasped the meaning of the first publications of the importance of basic CPR, and we fail to implement the knowledge of the importance of chest compressions and ventilations into our clinical practice. The early reports of the importance of attempting to defibrillate as soon as possible, resulted in under-emphasis on basic CPR, and the fate of patients without VF was largely forgotten.

In conclusion, the answer to the question in the title is Yes; survival has improved – from virtually zero fifty years ago to somewhere between 1-15% today. In this paper I have discussed briefly the problems related to comparison of different populations with regards to co-morbidity and medications in 1957 and 2007 and the problems inherent in all emergency medicine research; what is the appropriate denominator? The five milestones in cardiac arrest research that should have improved survival have been identified, and if I shall speculate on what will intervention or device that shall improve survival in the next decade, I will suggest that the biggest and easiest improvement would result from implementing current knowledge. The basic steps of chest compressions and ventilations are needed to maintain some perfusion and oxygenation in the brain long enough to restart the heart by defibrillation or by reversing the pathophysiology. Maybe this is best implemented with a mechanical chest compression device that doesn't get tired or distracted. Reperfusion initiates the detrimental cascades, and systematic intensive care is needed to obtain the best possible neurological outcome for these patients. Maybe neuroprotection with hypothermia or some new agent should be instituted before reperfusion even in the out-of-hospital setting for the best effect.

Previous publication

This paper is a revised version of my trial lecture on a prescribed topic given as part of the public disputation for the degree of PhD at the Faculty of Medicine, University of Oslo, presented on June 13th 2007. The original title for the trial lecture was: “Have revisions of CPR guidelines or other interventions improved survival after out-of-hospital cardiac arrest during the last 50 years?” The adjudication committee consisted of Prof. Mareet Castrén (Karolinska Institute, Stockholm, Sweden), Ass. Prof. Eirik Skogvoll (NTNU, Trondheim, Norway), and Prof. Johan Ræder (Ullevål University Hospital, Oslo, Norway).

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Conflict of interest

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