

# Cardiac arrest outside and inside hospital from a 30-year perspective in the Municipality of Gothenburg

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## ABSTRACT

**Aims:** 1: To describe the epidemiology of both out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA) in the Municipality of Gothenburg. 2: To describe the differences and similarities in cardiac arrest inside and outside hospital. 3: To describe the eventual change in outcome following the implementation of mechanical chest compression in the emergency medical service.

**Method:** Consecutive OHCA cases in the Municipality of Gothenburg between 1980 and 2009 to which the emergency medical service responded were followed up to hospital discharge and at 1-month after the event for survival and neurological outcome according to the Utstein guidelines. Consecutive IHCA cases at Sahlgrenska university hospital between 1994 and 2006 to which the rescue team was called were followed up to discharge and at one month after the event for survival and neurological outcome according to the Utstein guidelines. We used the Swedish Cardiac Arrest Register for comparison.

**Results:** In the time period 1980 - 1999 there were 5270 resuscitation attempts in relation to OHCA of which 3871 were regarded as being of cardiac aetiology. The delay to defibrillation was short (8 minutes median) and 27 percent of the witnessed OHCAs and 12 percent of the unwitnessed OHCAs received bystander-CPR. In all, 8.8% survived to discharge. In the Utstein "golden standard" (bystander-witnessed cardiac arrest of cardiac aetiology found in ventricular fibrillation), 20 % were discharged from hospital. In the time period 1994 – 2002, the rescue team at Sahlgrenska University hospital was called 1570 times. In 71% of the cases, the patient had suffered a cardiac arrest. If the patients found in ventricular fibrillation were defibrillated within three minutes, survival to discharge was 63% if the IHCA occurred on a ward with ECG-monitoring capacity and 72% if the IHCA occurred on a ward without ECG-monitoring capacity. Of IHCAs between 1994 and 2001 (n=833) 37 per cent survived to hospital discharge,

and 86 percent of them were alive one year later. The survival after IHCA was three times higher compared with OHCA for shockable rhythms and seven times higher for non-shockable rhythms. Between 1992 and 2009, curve for the survival after OHCA had a U shape, with the highest survival at the beginning and at the end. During the last decade, there was an increase in survival which was associated in terms of time with an increase in the use of mechanical chest compression. However, other factors of importance for survival, such as bystander CPR and post-resuscitation care, also changed.

**Conclusion:** If patients with ventricular fibrillation are defibrillated within three minutes after collapse, the majority will survive. There are changes in survival after OHCA in Gothenburg over time with improvement and deterioration. The mechanisms behind these changes are not entirely understood, but a delay to start of treatment and post-resuscitation care are most probably important. Survival after IHCA is much higher than after OHCA, but this is not solely explained by a short time to the delivery of treatment.

**Keywords:** Cardiac arrest, heart arrest, mechanical chest compression, prognosis, out-of-hospital cardiac arrest, in-hospital cardiac arrest, Utstein, outcome, DNAR

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# 1 SAMMANFATTNING PÅ SVENSKA

Ungefär var sjätte timme räddas någon människa till livet efter ett plötsligt oväntat hjärtstopp i Sverige. Bara för 50 år sedan var dessa människor dömda att dö. Under de senaste 50 åren har det skett en fantastisk utveckling vad avser omhändertagande av denna patientpopulation.

I föreliggande avhandling beskrivs omhändertagande och utfall bland patienter som drabbas av plötsligt oväntat hjärtstopp i och utanför sjukhusets väggar i Göteborg ur ett 30 års perspektiv.

Det kan vara väl värt att nämna att de tre artiklar som belyser hjärtstopp innanför sjukhusets väggar de första i Sverige som på ett omfattande och systematiskt sätt beskriver denna population som drabbas av den mest fruktade komplikationen som vi känner till.

Det inträffade 3871 oväntade hjärtstopp i Göteborg i perioden 1980 – 1999. Av dessa 3871 överlevde 8.8 % och kunde skrivas ut från sjukhuset. I den undergrupp av personer som drabbades av kammarflimmer kunde var 5:e person skrivas ut från sjukhuset.

På Sahlgrenska sjukhuset var det 1115 patienter som drabbades av hjärtstopp under perioden 1994 – 2002. Av de patienter som hade kammarflimmer överlevde 63 % om de var på en EKG övervakad avdelning och 72 % om de var på en icke EKG övervakad avdelning om de behandlades med defibrillator (hjärtstartare) inom 3 minuter.

Totalt överlevde 37 % av alla patienter med oväntat hjärtstopp på Sahlgrenska i perioden 1994 – 2001 och 86 % av dem var fortfarande i livet ett år senare. I jämförelse mellan oväntat hjärtstopp på och utanför sjukhus sågs en 3 faldigt ökad överlevnad på sjukhus för patienter med en hjärtrytmstörning som kunde behandlas med defibrillator och en 7 faldigt ökad överlevnad för patienter på sjukhus med en hjärtrytmstörning som ej kunde behandlas med defibrillator. Överlevnaden efter hjärtstopp utanför sjukhus uppvisar en U-formad bild i tidsperioden 1992 – 2009, med en ökad överlevnad det sista decenniet som tidsmässigt sammanfaller med introduktionen av mekanisk hjärtkompression, men andra viktiga faktorer för ökad överlevnad såsom ökad HLR utförd av vittnen till hjärtstoppet och utökad och intensifierad eftervård på sjukhus har även ökat.

## 2 LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. **Fredriksson, M., J. Herlitz, and J. Engdahl**, *Nineteen years' experience of out-of-hospital cardiac arrest in Gothenburg--reported in Utstein style*. Resuscitation, 2003. **58**(1): p. 37-47
- II. **Fredriksson, M., Aune, S., Thorén, A-B., Herlitz, J.**, *In-hospital cardiac arrest--an Utstein style report of seven years experience from the Sahlgrenska University Hospital*. Resuscitation, 2006. **68**(3): p. 351-8
- III. **Herlitz, J., et al.**, *Very high survival among patients defibrillated at an early stage after in-hospital ventricular fibrillation on wards with and without monitoring facilities*. Resuscitation, 2005. **66**(2): p. 159-66
- IV. **Fredriksson, M., et al.**, *Cardiac arrest outside and inside hospital in a community: mechanisms behind the differences in outcome and outcome in relation to time of arrest*. Am Heart J, 2010. **159**(5): p. 749-56
- V. **Fredriksson, M.H., J. Lindqvist, J. Axelsson, C.**, *Outcome after out-of-hospital cardiac arrest in a community in an 18-year perspective*. Submitted for publication, 2011

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## 4 ABBREVIATIONS

OHCA	Out-of-hospital cardiac arrest
IHCA	In-hospital cardiac arrest
DNAR	Do Not Attempt Resuscitation
CPR	CardioPulmonary Resuscitation
CAD	Coronary Artery Disease
CHF	Congestive Heart Failure
LQTS	Long QT Syndrom
MET	Medical Emergency Team
EDC	Emergency Dispatch Centre
EMS	Emergency Medical Service
CPC	Cerebral Performance Category
AED	Automated External Defibrillator
ICU	Intensive Care Unit
CCU	Coronary Care Unit
BLS	Basic Life Support
PCI	Percutaneous Coronary Intervention
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
PEA	Pulseless Electrical Activity
MCCU	Mobile Coronary Care Unit
MICU	Mobile Intensive Care Unit
ECG	Electro CardioGram
ACLS	Advance Cardiac Life Support
RRS	Rapid Response System
ICD	Implantable cardioverter-defibrillator

## 5 INTRODUCTION



**Dr Claude Beck**

In 1947, a 14-year-old boy was admitted for sternal surgery due to a congenital funnel chest malformation. At the end of the operation, his pulse suddenly stopped and no blood-pressure could be obtained. The wound was reopened and the cardiac surgeon Claude Beck immediately initiated internal cardiac massage. Dr Beck gave one milligram of epinephrine intravenously without effect. The boy was attached to a mechanical ventilator through an intra-tracheal tube. Dr Beck gave continuous cardiac massage for the next 35 minutes, and during this time Dr Pritchard was called for. Dr Pritchard had been doing laboratory research on dog defibrillation, and he noticed the fibrillatory movement of the boy's heart. He then ran to the fourth floor and collected an ECG film developer, took a picture and went downstairs to the darkroom to develop the film. The film showed a classical pattern of ventricular fibrillation. Dr Pritchard asked a nurse to get the rusty defibrillator. Dr Beck took off his gloves and checked the parts of the defibrillator, put on his gloves and placed the electrodes in position. Dr Pritchard worked the switch and gave a short shock without success. They shocked the heart again and this time it reacted according to the lab-research pattern; it was first stunned and then very imperceptibly it began to beat again. Dr Beck injected procaine hydrochloride into the right ventricle,

massaged the heart for an additional five minutes. It was now obvious that the contractions were coordinated and fairly vigorous.

The chest was sutured after 20 minutes, and the intra-tracheal tube was removed 10 minutes later, after which the boy resumed respirations. Three hours after defibrillation the boy responded rationally to questioning. By eight hours, he was fairly alert. He was discharged from hospital 31 days after the cardiac arrest without any signs or symptoms of injury to the central nervous system. In a follow-up three months later, he displayed a considerable increase in exercise tolerance and a normal ECG.

This was the first recorded successful defibrillation[1] after a cardiac arrest and it spurred interest in electrical defibrillation, which continues to this time.

## **5.1 The epidemiology of sudden cardiac death**

The estimated incidence of Out-of-Hospital-Cardiac Arrest (OHCA) in which CardioPulmonary Resuscitation (CPR) is attempted in Sweden is about 5000 cases per year or about 55 cases per 100000 persons and year[2]. The corresponding figure for the whole of Europe is estimated at 275000 cases of OHCA treated by the Emergency Medical Services (EMS), which results in an incidence of 37,7 OHCA that were treated by the EMS per 100000 person-years[3]. The incidence for the United States of America is reported to be higher, 55 cases of OHCA per 100000 person-years[4].

The corresponding figure for In-hospital Cardiac Arrest (IHCA) is more ambiguous, since the patients in hospital are often subjected to a Do Not Attempt Resuscitation (DNAR) procedure. For example at Sahlgrenska University Hospital only 11 per cent of all cardiac arrests are eligible for resuscitation. We do not have a complete picture for the whole of Sweden, as not all the hospitals as yet report to our national registry. In the literature there is a reported incidence of 0,175 cardiac arrests per hospital bed and year[5], while other reports state one to five cardiac arrests per 1000 hospital admissions[6-8].

## **5.2 The definition of cardiac arrest**

There have been several definitions of cardiac arrest over time but, since the Utstein consensus conference in 1990, there is a reasonably clear definition which the scientific community supports.

The Utstein[9] definition of OHCA is the cessation of cardiac mechanical activity, confirmed by the absence of a detectable pulse, unresponsiveness and apnea/agonal/gasping respirations. For the purposes of the Utstein style, no comment on time or "suddenness" is recommended.

The definition of the IHCA in the Utstein manner[10] is more a description of different resuscitation interventions; defibrillation only, chest compressions only, airway intervention only or a combination of any of the interventions. This is elaborated to an Utstein definition of a complete in-hospital cardiac arrest:

- absence of a palpable pulse
- unresponsiveness due to any cause
- apnea, agonal respiratory attempts and artificial ventilation

## 5.3 Development of Utstein style guidelines



### **The Utstein abbey**

The Utstein guidelines were drawn up at the Utstein Abbey, located on a small island near Stavanger in Norway. This meeting was an absolute necessity, as the knowledge in the field of resuscitation was rapidly growing, but no widespread consensus on how to report data existed. In 1977, The American Heart Association® started supporting resuscitation activities. In Europe there were several organisations with different opinions on

resuscitation and, in 1989 the European Resuscitation Council was formed as a multidisciplinary group with representatives from the European Society of Cardiology®, the European Academy of Anaesthesiology, the European Society for Intensive Care Medicine and national societies.

The American Heart Association® and The European Resuscitation Council came together in June 1990 at the Utstein Abbey to discuss the problem of the lack of a standardised language in reports and the problems with the nomenclature.

The meeting was followed up by a second meeting in the UK in December 1990, where members of The Heart and Stroke Foundation of Canada™ and The Australian Resuscitation Council also participated. It was called the Utstein Consensus Conference, and now the document stating the uniform way of reporting data from OHCA was drawn up here and the nomenclature became standardised, to avoid the previous semantic differences in interpretation.

The goal was to create a document to follow so that all the active scientists in the field reported data in the same way. This would make it possible to compare data from different studies and draw relevant conclusions. This would then expand the knowledge in the field of resuscitation and thereby improve the outcome.

## **5.4 The difference between sudden cardiac death and cardiac arrest**

A sudden cardiac death event is a more conceptual description of an unexpected cardiac arrest among patients with and without known heart diseases that always leads to death. In these cases an underlying heart disease is thought to be present.

The term cardiac arrest is a broader term to describe the event of a cardiac arrest, regardless of aetiology.

## **5.5 The arrhythmia behind sudden cardiac death**

Cardiac arrests are often divided into two groups, shockable and non-shockable rhythms. These rhythms are based on the first recorded ElectroCardioGram (ECG) after collapse. This is a practical way of dividing

cardiac arrests in a similar way as ST-elevation myocardial infarction and non ST-elevation myocardial infarction, since this selection is based on treatment principles. With the increasing implementation of public Automated External Defibrillators (AED), which interpret the rhythm in a dichotomous fashion as shockable/non-shockable, we have found a way to obtain an earlier rhythm recording than the recording made by the EMS following the arrival of the ambulance.

Patients found in a shockable rhythm have a much better prognosis if they are defibrillated early[11], hence the term shockable, which means that it is meaningful to give the heart an electric shock and the earlier the better.

In the group of patients found in non-shockable rhythms, the treatment is based on CPR. In this condition the basic manual CPR is the first line of treatment.

In the Utstein manner of reporting cardiac arrest[9, 10], the rhythm analysis is more electro-physical. The rhythm is divided into ventricular fibrillation, ventricular tachycardia without a detectable pulse, asystole and other rhythms which includes Pulseless Electrical Activity (PEA). This might be a good thing from a scientific point of view, since these four categories of arrhythmia represent a different pathophysiology and thereby a different treatment in many cases[12]. In overall terms, the prognosis among patients found in a non-shockable rhythm is very poor. Some reports suggest a different outcome after PEA as compared with asystole[13, 14], but others do not[5, 15].

## **5.6 The etiology behind sudden cardiac death**

The aetiology behind cases of sudden cardiac death is reported to be Coronary Artery Disease (CAD) in 80 percent, cardiomyopathies in 10 – 15 percent and other conditions eg Brugada, Congestive Heart Failure (CHF), Long QT Syndrome (LQTS) in about 5-10 per cent according to Chugh et al. [16].

## **5.7 The etiology behind cardiac arrest, where CPR was attempted**

There is a tendency to ascribe the majority of sudden non-traumatic deaths in middle-aged and elderly subjects to cardiac disease. However autopsy studies in unselected subjects suggest that about two-thirds of these deaths are cardiac in origin, with coronary artery disease and its complications accounting for the overwhelming majority of deaths[17].

Wennerblom and Holmberg in Gothenburg, found that 51 per cent of OHCA cases were due to ischemic heart disease[18]. More recently published studies from Finland 1996[19] and Germany 1997[20] report a range of 65 – 89 per cent of cardiac aetiology.

According to Priori et al.[17], reliance on death certificate diagnoses resulted in an underestimation of the true CAD rates of about five per cent.

Non-cardiac aetiologies are often overlooked or difficult to diagnose initially. Kuisma et al.[21] report that non-traumatic bleeding, pulmonary embolism, malignancy, intracranial processes, trauma, intoxication, drowning and choking are the most common non-cardiac causes of cardiac arrest.

## 5.8 The development of the mobile coronary care unit



**Dr Leonard Cobb**



**Dr James Francis Pantridge**

The first steps in the pre-hospital resuscitation of cardiac arrest were taken by Dr Pantridge in Belfast, Northern Ireland in 1966, with the introduction of a Mobile Coronary Care Unit(MCCU)[21]. He showed that, with CPR and a defibrillator in a physician-staffed ambulance, he was able to prevent death among patients suffering a cardiac arrest due to myocardial infarction, in such a way that far more of them could now be brought in to the emergency room alive.

This was followed up at first in the USA, by Leonard Cobb. He elaborated the idea of the MCCU, and staffed the ambulances with paramedics, a new kind of health-care providers who were basically fire-fighters with specific training for the mission. In collaboration with the fire department, they started the two-tier ambulance system, which brought CPR quickly to the scene, buying time for the ambulance with the defibrillator to arrive.

In Sweden a seven-week formal course in pre-hospital emergency care was started in the end of the 1960s and, in 1978, this course was mandatory(SOSFS 1978:34) for employment at the ambulance service.

The County of Gothenburg pushed the development of pre-hospital emergency care in Sweden forward when it deployed a hospital based MCCU in 1973. This was a single ambulance that was hospital-based and staffed with two Coronary Care Unit (CCU) nurses and two drivers. The MCCU was

dispatched when the suspicion of a cardiac emergency was reasonably high, as part of a randomised study of the effect of an MCCU versus standard ambulances on early mortality from ischaemic heart disease[23]. This system was operational until a re-organisation changed it into a Mobile Intensive Care Unit (MICU), in a two-tier system which was called out to all suspected emergencies. It was staffed by two paramedics around the clock and partly by a CCU nurse. The introduction of the MICU reduced the delay from the collapse to alarm, start of CPR and defibrillation[24].

## **5.9 The development of the resuscitation work within a hospital**

At Sahlgrenska University Hospital the development of a structured resuscitation team for IHCA dates back to 1966. Peatfield et al report in the Lancet in 1977[25] that the survival rate at their hospital in London was 8,7 per cent during the last decade, after an IHCA, CCU and Intensive Care Units (ICU) were excluded. From Burbanks, California Dr Coskey reports an increase in survival to discharge after IHCA from 16 per cent in 1965 to 32 per cent in 1974, pointing out the importance of a CPR-training programme and CCU[26].

In Sweden national standardised courses in CPR started in 1983[27]. In 1988 Advanced Cardiac Life Support (ACLS) courses started as an educational programme for nurses and physicians at ICU, CCU, emergency departments and operating wards[28]. This was later expanded to include the health-care CPR (H-CPR) in 2006[29], where the target group was now doctors wards of all kind and health care providers of all types. The goal is that CPR should be started within one minute after a cardiac arrest, for all persons eligible for resuscitation (not DNAR) at all locations in the hospital and all patients should be defibrillated within three minutes. A Swedish network of CPR coordinators was started in 2004, and in 2008, 93 percent of the Swedish hospitals had a dedicated person who was responsible for the hospital CPR training[30]. At Sahlgrenska University Hospital, there is a CPR centre which is also responsible for the Swedish national cardiac arrest registry.

Others, such as Moretti et al., showed that in-hospital ACLS training increased both short and long-term survival following IHCA[31].

In later years, the concept of the medical emergency team (MET) has been developed, with the purpose of interacting and pro-acting to avoid IHCA, in the conjunction with the early signs of critical illness. The MERIT study concluded that the introduction of the MET increased the overall number of

calls for the emergency team, but without any real effect on the incidence of CA, unexpected death or unexpected ICU admissions[32]. In Pittsburgh, Galhotra et al. reported that, in spite of having a MET/RRS(Rapid Response System), 18 per cent of all IHCAs were deemed to be "potentially avoidable", due to failure to adhere to established hospital patient care guidelines or policy; inadequate monitoring or surveillance; or delays in dealing with patient needs including delay in MET/RRS activation[33]. Other studies on the subject of MET have reported a reduction in IHCA incidence [34] and a reduction in mortality among these cases[35-37].

## **5.10 Cardiac arrest in relation to whether it took place outside or inside hospital walls**

The definition of a cardiac arrest is easier to make in an out-of-hospital setting. The Utstein definition is “the cessation of cardiac mechanical activity...confirmed by the absence of a detectable pulse, unresponsiveness and apnea (or agonal respirations)”[9]. This is a straightforward definition which is fairly easy to follow.

The in-hospital setting is much more complex. The patients can be in a mechanical ventilator or could have breathing difficulties that are not associated with cardiac arrest and they could also have various signs of cardiac dysfunction that may mimic a cardiac arrest. Since the patients are already hospitalised, the co-morbidity is expected to be higher and more severe, i.e. there are more acute and chronic conditions that might or might not influence the resuscitation outcome and the decision to start or not start resuscitation (DNAR). One example is the patient with prolonged asystole, where health care providers sometimes start CPR, when there is still some uncertainty about the presence of a pulse. It has been suggested that a non-cardiac aetiology behind the cardiac arrest is more common inside hospital walls than outside[38]. The definition of the IHCA in the Utstein way is therefore more a description of different resuscitation interventions; defibrillation only, chest compressions only, airway intervention only or a combination of any of the interventions. This is elaborated to produce an Utstein definition of a complete IHCA:

- absence of a palpable pulse
- unresponsiveness due to any cause
- apnea, agonal respiratory attempts and artificial ventilation

## 5.11 Why has the progress of resuscitation been slower inside than outside hospital?

The OHCA's are handled by two organisations with very clear guidelines, the Emergency Dispatch Centre (EDC), which receives the call about the presumed collapse and is responsible for alerting the EMS. The EMS is responsible for dispatching an ambulance and starting resuscitation and thereafter transporting the collapsed person to the emergency room at the hospital. Everyone has a very clear role and goal in these organisations. The IHCA's are handled by the ward staff, the switchboard and the resuscitation team. The resuscitation team consists of a variety of constellations, but frequently three different doctors. They are on call according to separate schedules, so the group of individuals is constantly changing, thereby preventing the team being well trained together, although the qualifications of every doctor are high. There is also a greater risk of misunderstanding if the group is not perfectly clear about the internal responsibilities, who takes care of what. In principle, it would be true to say that the treatment of an OHCA was built into the system from the beginning. This was not the case for IHCA's. In this case, so many disciplines are involved and no one takes responsibility. A practical example is the sad fact that, in 1990, Stig Holmberg, one of the heads of the Department of Cardiology at Sahlgrenska University Hospital, threatened to sue the present hospital executive board, if he discovered further patients in whom CPR had been neglected and not started at the earliest possible time (Stig Holmberg, personal communication). Only then did the department receive the resources to begin the systematic education of the hospital staff in CPR. During the last two decades we have seen constructive work on building organisations to handle IHCA in a large number of hospitals in Sweden[30].



**Dr Stig Holmberg**

## 6 AIMS

- To describe 20 years' experience of out-of-hospital cardiac arrest in Gothenburg according to the Utstein guidelines
- To describe seven years experience of in-hospital cardiac arrest at Sahlgrenska University Hospital in Gothenburg according to the Utstein guidelines
- To describe survival after in-hospital cardiac arrest among patients found in ventricular fibrillation with the emphasis on delay to defibrillation
- To compare the characteristics and outcome after cardiac arrest where cardiopulmonary resuscitation was attempted out of hospital and in hospital in Gothenburg during a period of years
- To describe the outcome from out-of-hospital cardiac arrest in Gothenburg from an 18-year perspective with the emphasis on the implementation of mechanical chest compression

## **7 PATIENTS AND METHODS**

### **7.1 Out-of-hospital cardiac arrest Study area and population**

Gothenburg is the second largest city in Sweden in terms of population. The resident population in 1980 was about 430000 and this figure has increased moderately to total about 513000 today. In 1999, the population was about 462000 of which 49% were men and almost 16% were 65 or older.

In Gothenburg in 1996, twenty-four percent of all deaths were due to ischemic heart disease.

The total death incidence was 1116 deaths / 100000 inhabitants and year in Gothenburg in 1996.

The number of people who completed a CPR course initiated and carried out by instructors educated by the CPR-centre at Sahlgrenska univeristy hospital in 1996 – 2000 totalled 18873. The total figure is probably higher, as we do not have access to other educators' figures, e.g. the number of people educated by the Red Cross Organisation.

### **Emergency Medical Service**

During the study period the EMS has undergone many changes, both structural and medical. The EMS was a two-tier system during the study period. At the beginning of the study period, the first tier was staffed by Emergency Medical Technicians (EMT). The AED was gradually implemented in the first tier between 1987 and 1991. The second tier is an ALS-equipped unit, which was crewed by two paramedics and, from 1985, also by a nurse, during the daytime on weekdays. Since 1997, there has been one full-time paramedic and one nurse.

One major structural change took place in 2003, when the ambulance service was contracted out to a private contractor on behalf of the municipality.

### **Emergency Dispatch Centre (EDC)**

The emergency dispatch centre has also undergone changes during this long period; for example, a new nationwide emergency number standardised for

the whole of the European Union (EU) has been implemented, telephone-assisted CPR has been introduced and the educational level of the staff at the dispatch centre has increased dramatically.

The dispatcher receiving the call interrogates the caller using a formal protocol. While interrogating the caller, the dispatcher uses a computerised system to instruct a colleague to dispatch an ambulance.

## **Time recording**

Prior to 2004, the ambulance crew asked the witnesses for the time of arrest and when the call to the EDC took place. They then added the times measured by themselves at the scene to obtain a total time framework for the event.

In 2004, a computerised system that keeps track of all times from the call received by the EDC to the point at which the ambulance arrives at the scene was introduced. To avoid inter-clock differences in the OHCA setting all time intervals are taken from a single clock once the ambulance is at the scene.

## **Data acquisition**

The data acquisition method has changed during the study period. From 1980 until November 2007 there was a paper-based system, starting from the EMS logbook in which the background data of the patients who had undergone a resuscitation attempt were collected. We then collected the data for each case from the ambulance trip sheet, the hospital records and death certificates. All the data were written in a formal report and entered manually into a computerised database. From November 2007 there was a change to a web-based system for easier handling of data.

## **The compression/decompression CPR device – LUCAS™**

The active compression/decompression method was developed in a mechanical device called the LUCAS(Lund University Cardiac Assist System)™device. The LUCAS™device is a gas- or battery-driven CPR device providing mechanical active compression decompression-cardiopulmonary resuscitation.

The EMS has implemented the LUCAS™ device, for a technical description please see the website <http://www.jolife.se/en/products>

It has previously been shown that the LUCAS™ device is better than regular CPR in pig models [39, 40], produces higher end tidal carbon dioxide levels in humans [41] and provides better metric changes in the ECG signal (which indicates a higher success rate after defibrillation) [42]. The quality of CPR is better with the LUCAS™ device than regular CPR before and during transportation [43], it is safe to use in an out-of-hospital location [44] and appears to be associated with the same incidence and variety of injuries as manual CPR [45]. However, the latter question requires larger confirmatory studies.

## **7.2 In-hospital cardiac arrest**

### **Settings**

Sahlgrenska University Hospital (SU) is a primary/secondary/tertiary hospital. The hospital is divided into three different locations; Sahlgrenska (SU/S), Östra (SU/Ö) and Mölndal (SU/M). SU/S serves both a local population of about 600000 as a primary/secondary hospital and a regional population of about 1500000 as a tertiary hospital. During the study period the number of beds and wards at SU/S has changed, but there is an average of about 900 beds, 24 beds in the ICU and 38 beds in the CCU of which four have ICU capacity.

### **Resuscitation team and equipment**

At Sahlgrenska University Hospital, a designated resuscitation team is available 24/7. It is composed of a cardiologist, an anaesthesiologist and a specialist in internal medicine. The ICU and CCU are equipped with manual defibrillators, while the other wards have AEDs. Every ward has its own standardised emergency equipment, with drugs, an intubation kit and so on. At the time of the survey, all hospital staff were regularly trained in basic life support (BLS) and all the medical staff were also trained to use the AEDs. The nurses at the ICU and CCU also received training in manual defibrillation.

## **Resuscitation alert**

Sahlgrenska Hospital has a designated telephone number, which goes directly to the switchboard. The telephone operator alerts the resuscitation team, who report to the switchboard and are given the location of the arrest. The telephonist notes the time and date, the ward number and personal identification number of the patient on a specific list. These lists are later collected by the CPR centre for analysis and follow-up.

## **Do not attempt resuscitation (DNAR)**

The senior physician on the ward decides on DNAR in consensus with the patient or relatives and the ward staff. The decision is stated in the hospital record, as a dynamic, on-going decision which may be modified according to the patient's medical progress.

## **Data acquisition**

Until 2005, the data on patients, what was done and where the event took place came from three different sources: the list from the telephone switchboard, the standardized report filled in by the ward nurse and the standardised report filled in by the cardiologist on the resuscitation team. The data were then collected in the report sent in to the Swedish Cardiac Arrest Register[39], which was web based already from the beginning in 2005.

## **Time recording**

The responsible nurse on the ward measures the time intervals, using one watch to avoid inter-clock differences.

## 7.3 Cerebral performance category(CPC)

The preferred way of measuring cerebral outcome after cardiac arrest is the CPC. It is reported in five simple steps, of which categories one and two are considered to be relatively good cerebral outcome.

1. Good cerebral performance. Conscious. Alert, able to work and lead a normal life. May have minor psychological or neurological deficits (mild dysphasia, non-incapacitating hemiparesis, or minor cranial nerve abnormalities).
2. Moderate cerebral disability. Conscious. Sufficient cerebral function for part-time work in a sheltered environment or independent activities of daily life (dressing, travelling by public transportation and preparing food). May have hemiplegia, seizures, ataxia, dysarthria, dysphasia or permanent memory or mental changes.
3. Severe cerebral disability. Conscious. Dependent on others for daily support because of impaired brain function (in an institution or at home with exceptional family effort). At least limited cognition. Includes a wide range of cerebral abnormalities from ambulatory with severe memory disturbance or dementia precluding independent existence to paralytic and able to communicate only with eyes, as in the locked-in syndrome.
4. Coma, vegetative state. Not conscious. Unaware of surroundings, no cognition. No verbal or psychological interactions with environment.
5. Death. Certified brain dead or dead by traditional criteria.

## 7.4 Statistical analyses used in Papers I – V in the thesis

	Paper I	Paper II	Paper III	Paper IV	Paper V
<b>Comparison between two groups</b>					
<b>Dichotomous variables</b>					
Fisher's exact test	X				
Chi-2				X	
Mann-Whitney U-test					X
<b>Continuous variables</b>					
Fisher's non-parametric permutation test	X	X	X		
Student's 2-sample t-test				X	
Spearman's rank correlation					X
<b>Multivariate analysis</b>					
Logistic regression models, adjusted for baseline variables				X	
Box-Tidwell test				X	
Hosmer-Lemeshow				X	
EM algorithm				X	

# 8 RESULTS

I:



Resuscitation 58 (2003) 37–47



## Nineteen years' experience of out-of-hospital cardiac arrest in Gothenburg—reported in Utstein style

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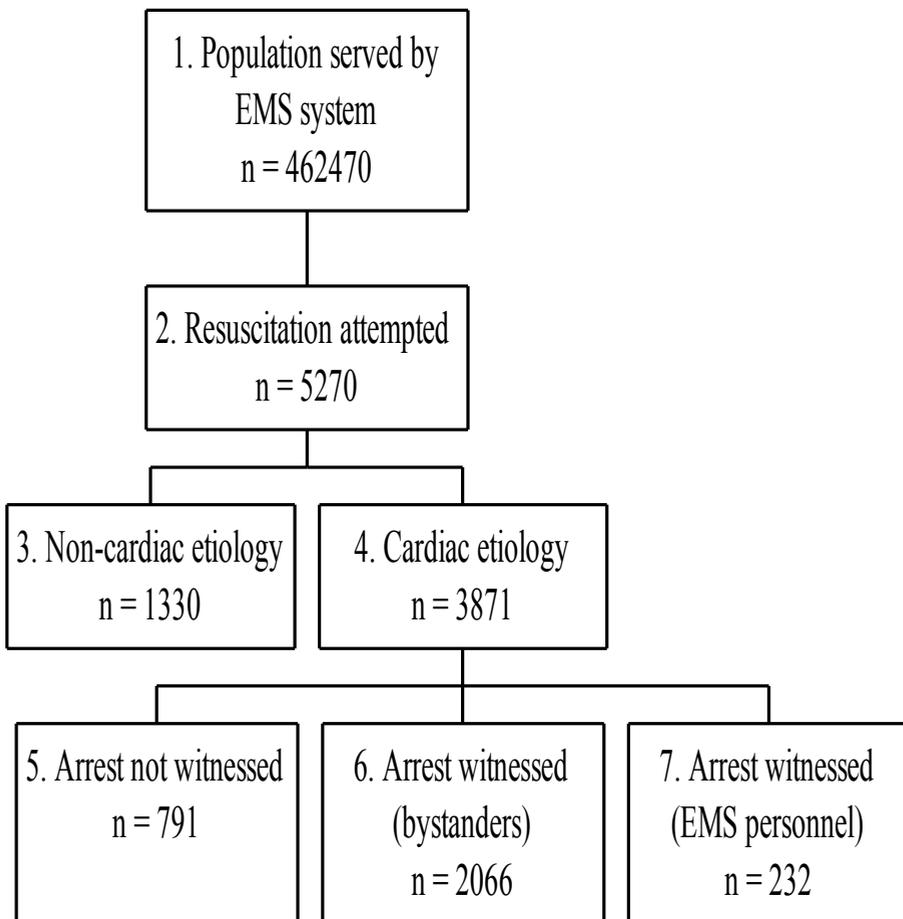
### Objective

To describe the outcome in the Utstein style for out-of-hospital cardiac arrest in Gothenburg, over a period of 19 years.

# General results; Utstein template 1:

During the 19 years (1 October 1980 to 31 August 1999) that were studied, resuscitation was attempted 5270 times and 73 per cent (n=3871) of the arrests were of cardiac aetiology. Of these cases, 67 per cent were bystander witnessed (n=2066).

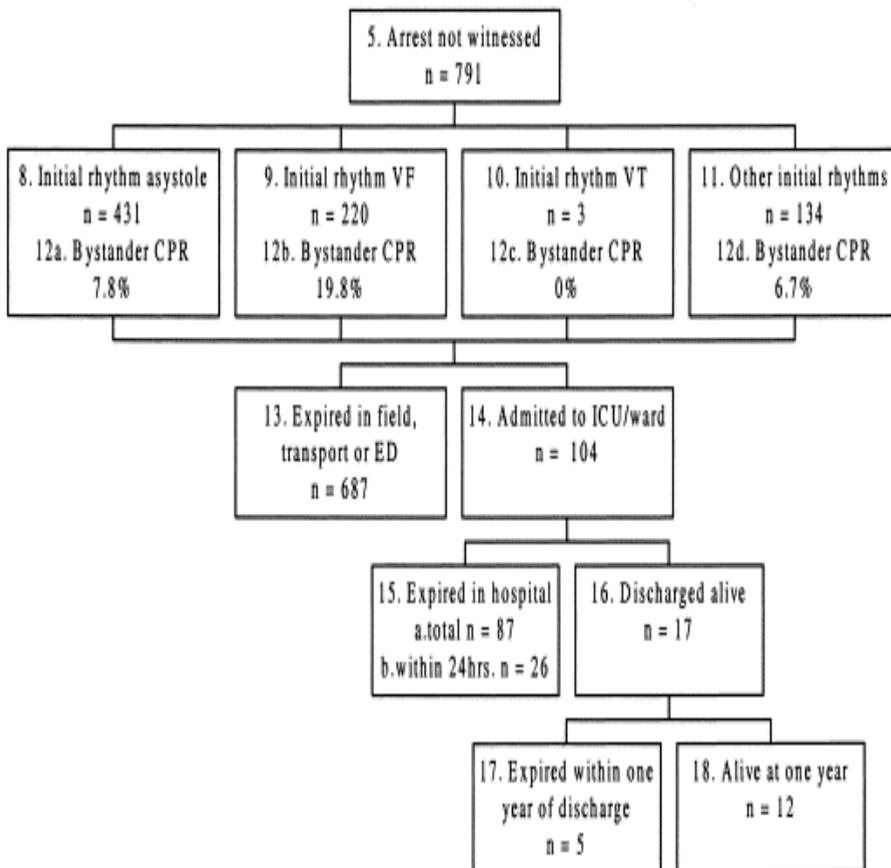
## Template 1: General results



# Unwitnessed cardiac arrest;

## Utstein template 2:

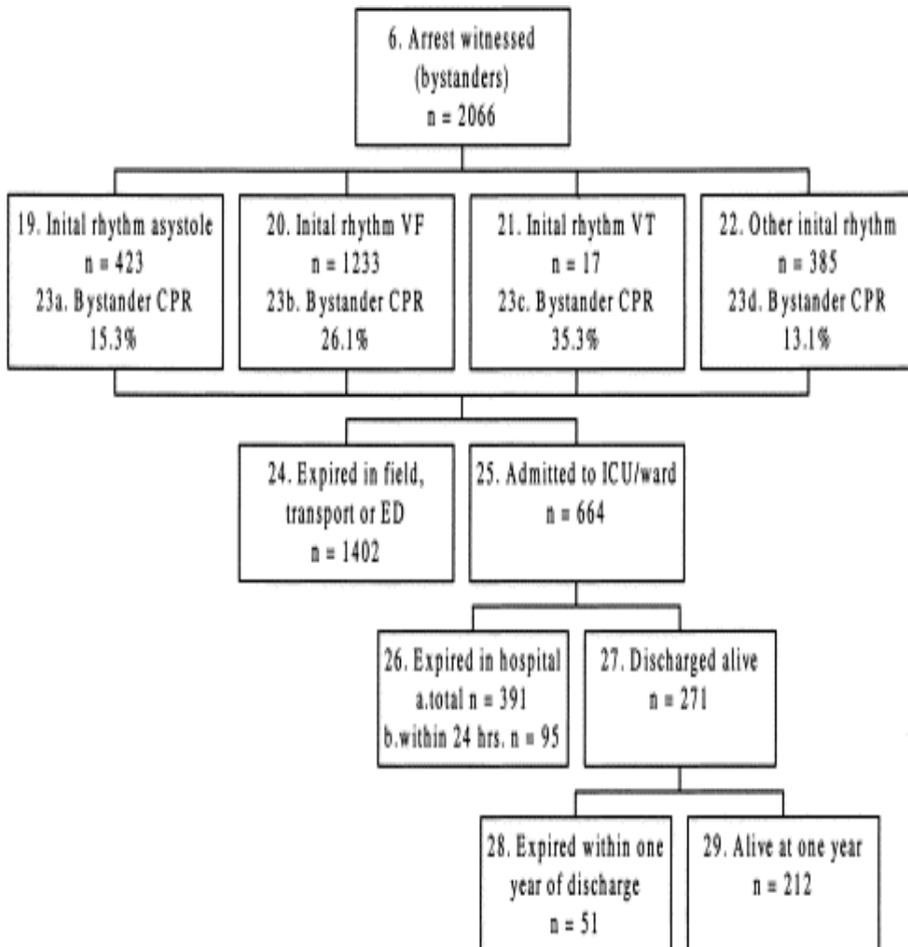
If the arrest was unwitnessed (n=791) asystole was the most common initial rhythm, reported in 54 percent (n=431) of the cases, while ventricular fibrillation was reported in 28 per cent (n=220). The overall survival to discharge from hospital for a patient suffering an unwitnessed cardiac arrest of cardiac aetiology was two per cent (n=17).



# Bystander-witnessed cardiac arrest;

## Utstein template 3:

If the cardiac arrest was witnessed by a bystander, the most common initial rhythm was ventricular fibrillation – 60 per cent (n=1233) of the cases. The overall survival to discharge was 13 per cent (n=271).

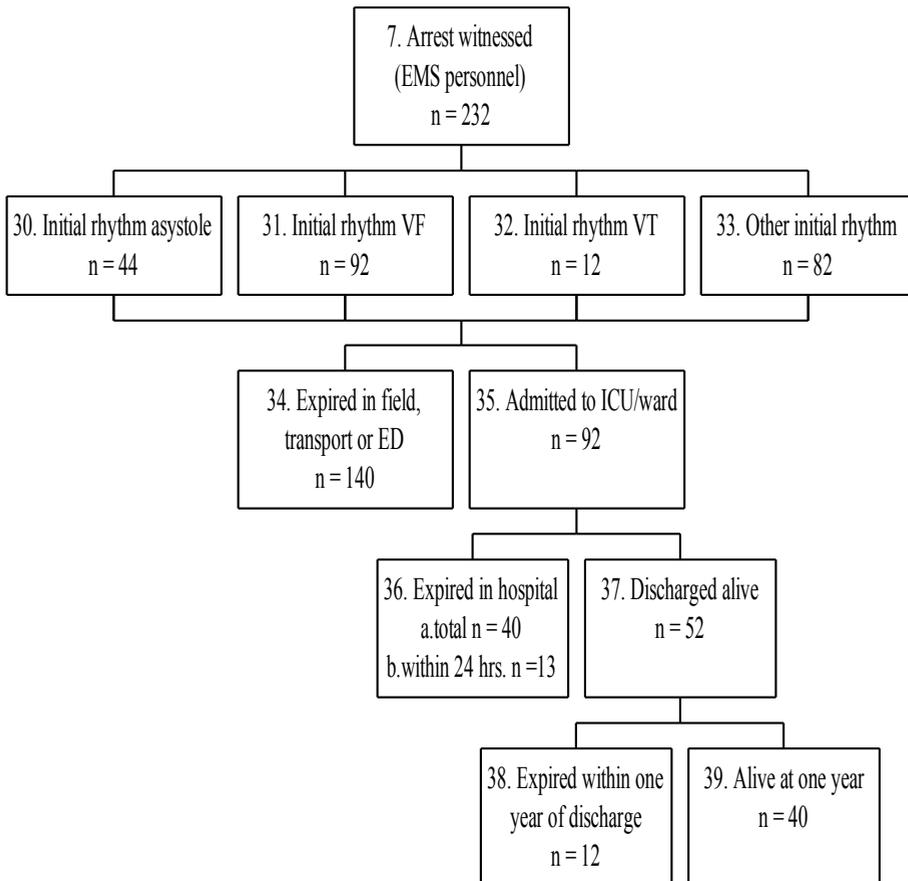


# EMS–personnel–witnessed cardiac arrest;

## Utstein template 4:

Ventricular fibrillation was the most common rhythm for these patients, reported in 40 per cent (n=92) of the cases. The overall survival to discharge was 22 per cent (n=52).

Template 4. EMS-personnel witnessed arrest



## **Conclusion:**

In this large Utstein-style study of OHCA stretching over almost 19 years, we report high survival rates both for patients suffering a bystander-witnessed cardiac arrest and for the subgroup suffering a bystander-witnessed cardiac arrest with VF as the first recorded rhythm. These high survival rates can in part be explained in part by the short time intervals from calls being received by the EDC to the arrival of the EMS at the scene.

II:

Resuscitation (2006) 68, 351–358



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## In-hospital cardiac arrest—An Utstein style report of seven years experience from the Sahlgrenska University Hospital<sup>☆</sup>

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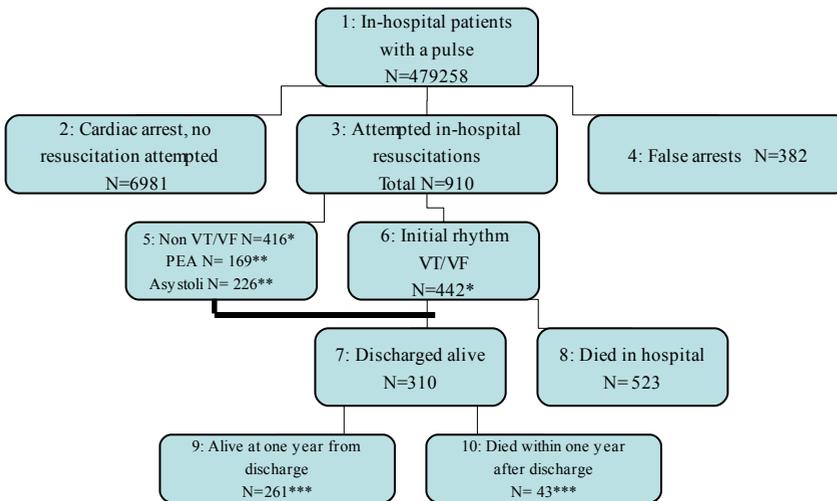
Received 4 March 2005; received in revised form 5 July 2005; accepted 15 July 2005

### Objective

To describe seven years' experience of IHCA at Sahlgrenska Hospital in Utstein style, with a primary endpoint of survival to discharge

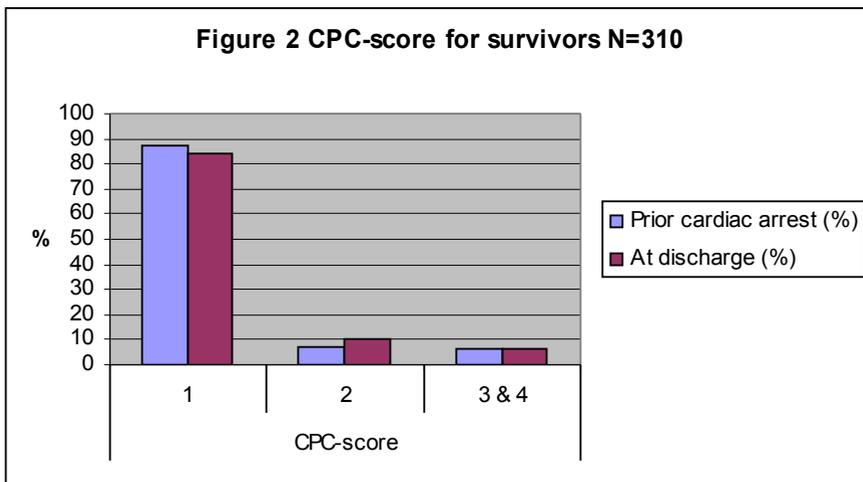
# Results: the in-hospital Utstein template

The overall survival to discharge was 34 per cent (n=310). The vast majority of patients who died in hospital died within 24 hours (83 per cent).



# CPC score before and after the cardiac arrest

The figure shows the distribution of patients who survived to hospital discharge according to CPC score on admission and at discharge from hospital. The patients surviving their cardiac arrest had no deterioration in CPC score.



## Diagnosis at admission

Almost one third of the patients with IHCA were admitted to hospital due to an acute myocardial infarction. Almost two thirds were admitted due to cardiac related diagnoses.

## Health history on admission to hospital

Nearly half the patients had a history of angina pectoris, one third had a history of myocardial infarction and one fifth of the cardiac arrest cases had a history of diabetes prior to the event.

## **Utstein golden standard**

For the patients suffering a witnessed cardiac arrest found in ventricular fibrillation of cardiac aetiology, the survival rate rate to discharge was 59 per cent.

## **Conclusion**

We report a high survival rate for IHCA. We have pointed out that a functional chain of survival, short intervals before the start of CPR and defibrillation are probably strong contributory factors to this finding.

III:



Resuscitation 66 (2005) 159–166

RESUSCITATION



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## Very high survival among patients defibrillated at an early stage after in-hospital ventricular fibrillation on wards with and without monitoring facilities<sup>☆</sup>

Johan Herlitz\*, Soveig Aune, Angela Bång, Martin Fredriksson, Ann-Britt Thorén, Lars Ekström, Stig Holmberg

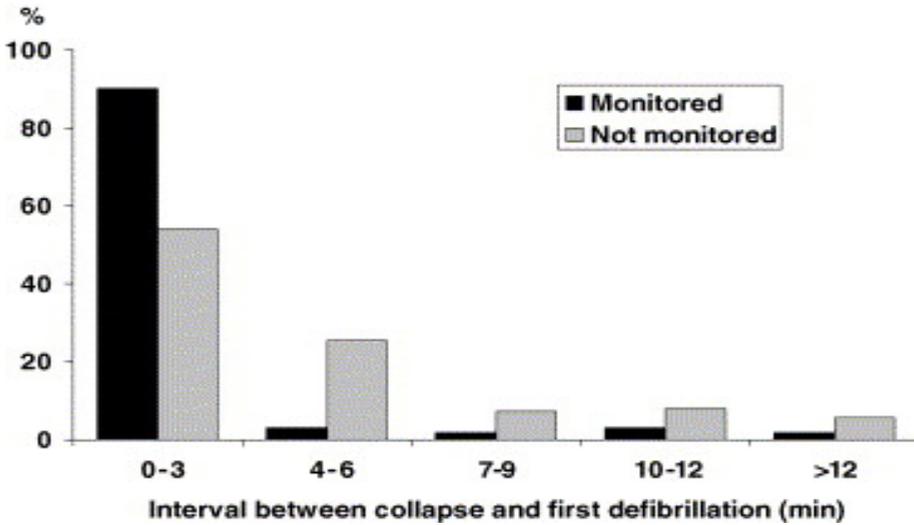
*Division of Cardiology, Sahlgrenska University Hospital, SE-413 45 Göteborg, Sweden*

Received 30 September 2004; received in revised form 23 March 2005; accepted 24 March 2005

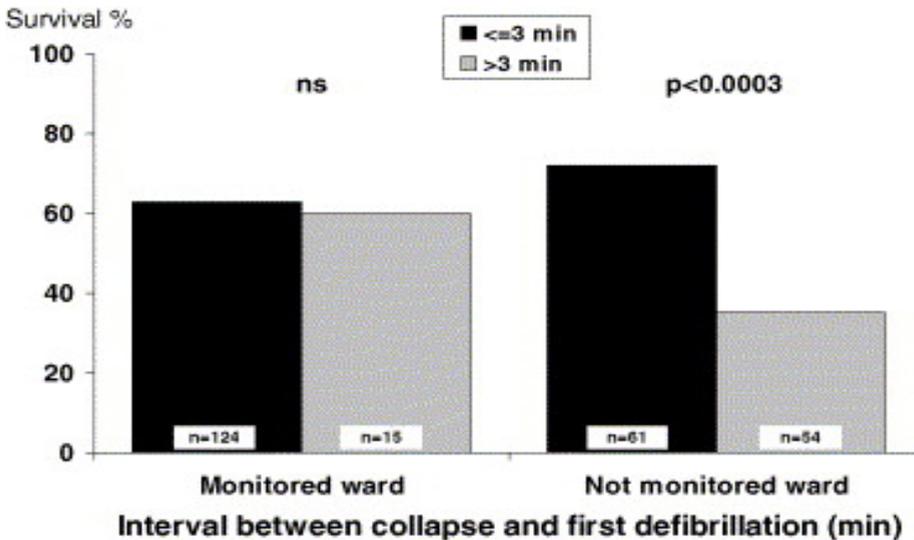
### Objective

To describe the outcome for patients who suffered an IHCA and were found in ventricular fibrillation with the emphasis on the delay to defibrillation.

# Results



IHCA on monitored wards is defibrillated faster than IHCA on non-monitored wards.



Defibrillation within three minutes clearly improves survival on non-monitored wards.

## **Conclusion:**

If patients with in-hospital ventricular fibrillation were defibrillated early on both monitored and non monitored wards, survival to hospital discharge was high. This highlights the importance of being prepared for rapid defibrillation on wards without monitoring facilities.

## IV:

### **Cardiac arrest outside and inside hospital in a community: Mechanisms behind the differences in outcome and outcome in relation to time of arrest**

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## **Objective**

To compare characteristics and outcome after cardiac arrest where CPR was attempted outside and inside hospital over 12 years in the municipality of Gothenburg.

## Results:

### Table: Patient characteristics

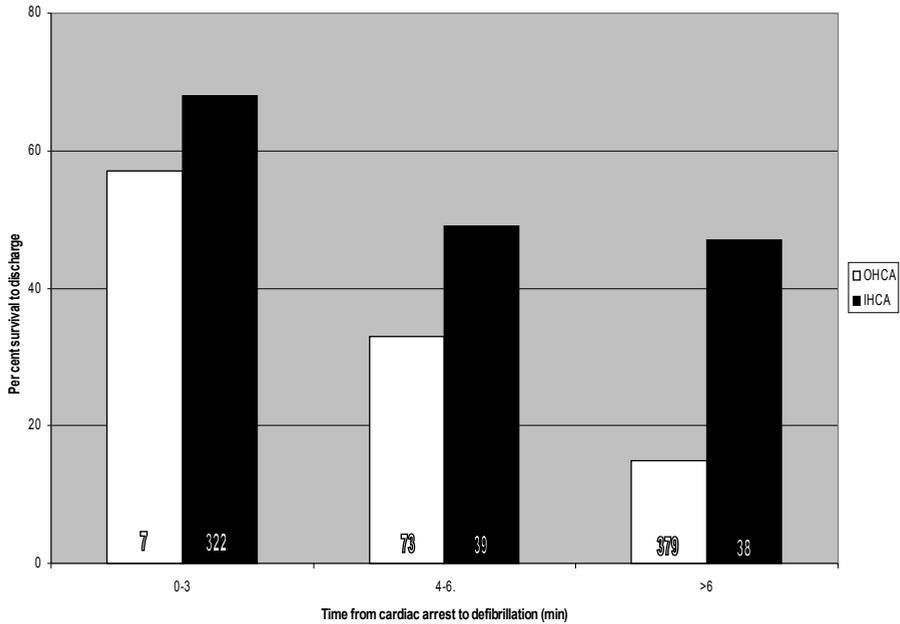
Patients with OHCA were somewhat younger and included fewer women. Patients with OHCA differed from patients with IHCA particularly with regard to delay, which were longer in OHCA, and the occurrence of ventricular fibrillation as the initial observed arrhythmia, which was more frequent after IHCA. A witnessed cardiac arrest was also more frequent in IHCA. Treatment with intubation and adrenalin was more frequent after OHCA.

	<b>OHCA</b>	<b>IHCA</b>	<b>p</b>
* No patients for whom information was available	<b>n=2,984</b>	<b>n=1,478</b>	
<hr/>			
<b>Age (years)</b> (2,835, 1,478)*			
Mean	68	69	0.005
Median	72	72	
<b>Gender (%)</b> (2,683, 1,478)			
Female (2,746, 1,328)	32	37	0.002
<b>Witnessed (%)</b>	70	92	< 0.0001
<b>Initial arrhythmia (%)</b> (2,817, 1,280)			
Ventricular fibrillation	31	50	< 0.0001
<b>Treatment (%)</b>			
Intubation (2,984, 1,363)	73	46	< 0.0001
Adrenalin (2,984, 1,381)	81	57	< 0.0001

## Table: Patient characteristics

	<b>OHCA</b>	<b>IHCA</b>	<b>p</b>
	<b>n=2,984</b>	<b>n=1,478</b>	
<b>Interval from cardiac arrest to (1,255)</b>			
Call for ambulance (min)			
Median	3	1	< 0.0001
25% and 75% percentiles	1 – 5	0 – 2	
<b>Arrival of rescue team (min) (1,199, 135)</b>			
Median	9	4	NA
25% and 75% percentiles	6 – 12	2 – 5	
<b>Defibrillation (min) (461, 401)</b>			
Median	10	1	< 0.0001
25% and 75% percentiles	7 – 13	0 – 2	

Figure 1



There was a strong association between delay from collapse to defibrillation and the chance of survival in both OHCA ( $p < 0.0001$ ) and IHCA ( $p = 0.0009$ ).

Among survivors, the CPC score was much better after IHCA than after OHCA. This finding was not explained by more severe co-morbidity among patients with OHCA as shown in the table on the next page.

## Table: Previous history among survivors in whom information on CPC score was available

Previous history	OHCA	IHCA
	n=232	n=570
	%	%
Diabetes	12	17
Myocardial infarction	33	36
Heart failure	23	28
Stroke	9	9

## Conclusion

Compared with OHCA, the survival of patients with IHCA increased threefold for shockable rhythm and sevenfold for non-shockable rhythm in our practice setting. There was a strong association between delay to defibrillation and survival in both OHCA and IHCA. If patients were found in a shockable rhythm, the higher survival after IHCA was only partly explained by a shorter delay to treatment. The time and day of CA were associated with survival in IHCA but not OHCA.

**V:**

**Outcome after out-of-hospital cardiac arrest  
in a community from an 18-year perspective –  
submitted for publication**

**Objective**

To describe the eventual change in outcome after OHCA in a community during a period of 18 years in relation to a successive increase in the use of mechanical chest compression.

**Results**

The sample was divided into four cohorts with an increased use of mechanical chest compression:

1. 1992-01-01 – 2003-05-21 (no mechanical chest compression)
2. 2003-05-22 – 2005-05-25 (25% had mechanical chest compression)
3. 2006-01-01 – 2007-12-31 (59% had mechanical chest compression)
4. 2008-01-01 – 2009-12-31 (64% had mechanical chest compression)

During the time period, the proportion of patients with a cardiac arrest witnessed by the EMS-crew increased, the proportion of bystander CPR increased and post-resuscitation care improved.

## Percentage of patients hospitalised alive

	1992–2003	2003–2005	2006–2007	2008–2009	p*
	n=2408	n=491	n=423	n=499	
All patients (n=3772) (49)**	29	30	33	37	0.006
<b>Initial rhythm</b>					
Shockable rhythm(n=1112)	44	50	54	62	0.0008
Non-shockable rhythm (n=2340)	22	21	24	28	0.06
<b>Witnessed status</b>					
Crew witnessed(n=489)	38	37	32	40	
Bystander witnessed (n=1968)	33	33	41	42	0.009
Non-witnessed(n=1016)	20	19	18	25	
<b>Aetiology</b>					
Cardiac(n=2367)	31	29	37	39	0.004
Non-cardiac(n=1081)	26	33	22	34	0.04

\* p-value denoted if < 0.20 \*\* Information on survival missing in 40, 6, 1 and 2 patients respectively

There was an overall increase in survival to hospital admission. The increase was particularly marked among patients found in a shockable rhythm, among those who were bystander witnessed and among those with a cardiac aetiology.

## Table: Percentage of patients surviving to one month

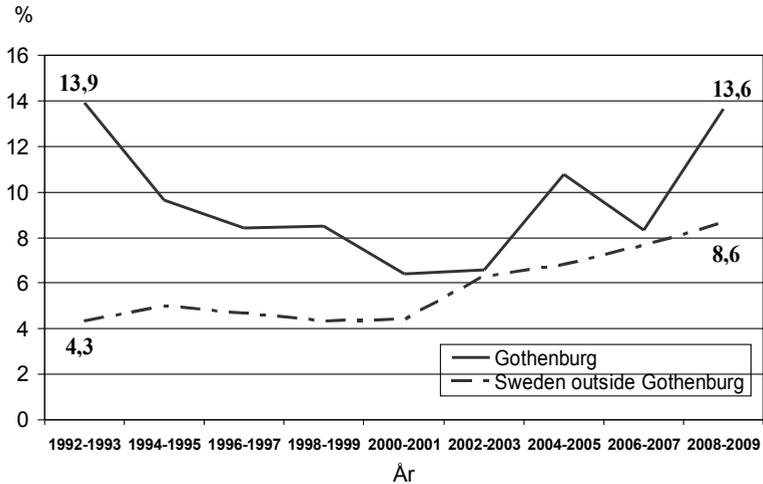
	1992–2003 n=2408	2003–2005 n=491	2006–2007 n=423	2008–2009 n=499	p*
<b>All patients</b> (n=3789) (32) **	8.6	9.4	8.3	13.6	0.004
<b>Initial rhythm</b>					
Shockable rhythm(n=1117)	18.3	25.6	24.3	35.7	< 0.0001
Non-shockable rhythm (n=2355)	3.4	3.2	2.5	5.5	0.14
<b>Witnessed status</b>					
Crew witnessed(n=483)	16.7	20.0	11.7	22.1	
Bystander witnessed (n=1980)	10.0	9.0	11.6	14.2	0.18
Non witnessed(n=1026)	3.8	4.2	1.1	5.5	
<b>Aetiology</b>					
Cardiac(n=2374)	9.6	10.0	10.8	15.4	0.02
Non-cardiac(n=1084)	6.5	8.4	4.0	10.9	0.10

\* p-value denoted if < 0.20 \*\* Information on survival missing in 28, 1, 2 and 1 patients respectively

There was an overall increase in survival to one month. The increase was found during the last period. The increase in survival was most marked among those found in a shockable rhythm.

However, as shown in the figure on the next page, survival was equally high at the beginning of the 1990's as it was in 2008-2009.

Fig 2



## Conclusion

During 18 years of OHCA in Gothenburg, there was an increase in the use of mechanical chest compression. During the time in which mechanical chest compression was implemented, there was an increase in survival. However, the association between an increase in the use of mechanical chest compression and survival could not be confirmed, as other factors may also have contributed.

## 9 DISCUSSION

### **Why is there a need for the Utstein template?**

The Utstein way of reporting is a milestone in modern cardiac arrest research. Before the Utstein guidelines were introduced, there was no consensus on the semantic values of cardiac arrest or many other important events in the OHCA field, for example [9]. So, before they were introduced, some authors only included patients with ventricular fibrillation in their reports whereas others did not. With the Utstein guidelines, we learned to describe patients according to aetiology, witnessed status and initial rhythm. It was in this context that the participants from the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, the Australian Resuscitation Council and the Resuscitation Councils of Southern Africa came together and formulated these guidelines. The goal was to create a standardised way of reporting data and thereby make it easier to compare data and drive knowledge and science forward. By standardising the nomenclature, the scientific community can focus on the different aspects that are known to influence outcome and find new ones, instead of debating how we should define a cardiac arrest and which parameters are important to measure and how.

### **What are the advantages and disadvantages of the Utstein template?**

The advantages of the Utstein template are obvious. It provides us with a means immediately to compare results with other published data, with the advantage of widespread standardisation and uniformity. The template shows all the key elements, but there is also a possibility for extra boxes, if one would like to elaborate on a specific part of the cardiac arrest event, e.g. in the Utstein guidelines for OHCA it is possible to analyse cardiac arrest of non-cardiac aetiology in the same fashion as the cases of cardiac aetiology[9].

The disadvantages of the Utstein template could be that exciting new ideas are boxed into the template system and not elaborated in the way that is necessary. Studies that do not conform with the Utstein template could be overlooked for this reason and important knowledge could therefore be

missed. It is also a possible that changes in the cardiac arrest background factors (i.e. new diseases causing cardiac arrest) or brand-new treatment models will simply not be best evaluated by the Utstein template. Although we have a uniform nomenclature, we still have a very large variety in outcome, which is not explained by the Utstein elements[40].

## **Which were the most important changes after OHCA in the long-term perspective?**

The concept of chain of survival [41] with its links that are joined to one another, remains the most important factor when it comes to obtaining the best possible survival after OHCA. Every link is important in itself, but, to achieve success, all of them must work as a fluent chain of events. The implementation of AED in the first-tier ambulance produced a steep increase in survival around 1990. This is probably the single most important positive thing that has meant the most when it comes to improving survival after OHCA in Gothenburg. However, there was also an increase in bystander CPR, which is an important factor for increased survival[42-43]. We also observed an increase in the proportion of crew-witnessed OHCA. This is important, as it might reflect a higher awareness in the community. This in turn might be an effect of educational efforts to make the public more alert to signs of cardiac illness, i.e. a tendency to alert the EMS at an earlier stage, so that the ambulance reaches the patient before the cardiac arrest. It has been suggested that the latter two factors, i.e. an increase in bystander CPR and an increase in crew-witnessed OHCA explain the overall increase in survival after OHCA in Sweden over time[44]. O'Keeffe et al. conclude that the chance of surviving an OHCA increases sevenfold if an ambulance crew arrives prior to the arrest [45].

During the time period we have also seen tremendous developments in post-resuscitation care. This includes the introduction of mild hypothermia, which has been shown to improve the neurological outcome[46-47], and the increasing use of percutaneous coronary intervention (PCI) that has been reported to be associated with both improved neurological outcome and survival[48-53]. However, no randomised clinical trial has confirmed the value of PCI in terms of survival after OHCA.

On the negative scale of important changes, we see a very troubling trend with an increase in time intervals from calling for an ambulance until the arrival of the ambulance at the scene. This is the result of a combination of factors; which will be discussed below. We have also seen a decline in the

proportion of OHCA with ventricular fibrillation as the first recorded rhythm, which is in line with other published results[54, 55].

## **Why was there an increase in EMS response time?**

The EMS response time has increased during the period. This is most probably due to multifactorial events, linked in part to one another.

Increased traffic; The city of Gothenburg is expanding and the traffic intensity is constantly growing. This is one of the reasons for the prolongation in EMS response times. There has also been a shift in management, as the ambulance service was previously owned by the municipality. Since 2003, the EMS has been contracted to a private corporation. This has been associated with higher occupancy and fewer ambulances free for immediate action, thereby giving them a longer drive to get to the patient. In combination with the higher traffic intensity, these are the most relevant factors in term of the increase in EMS response time. According to some EMS staff, lay persons in cars do not pay attention to ambulances in the same way as ten years ago (they listen to music and talk on mobile phones). Another factor that has been suggested is that the dispatchers give priority 2 instead of priority 3 to many more cases today than before in order to reduce the risk of under-prioritising cases. This increases the burden on the EMS.

## **Why was there a decrease in ventricular fibrillation?**

We observed an increase in the EMS response time and a decrease in the proportion of patients found in a shockable rhythm. These two observations are probably linked to one another as, with each minute that passes after a cardiac arrest, an increasing number of ventricular fibrillations have converted to a non-shockable rhythm[56]. It is also possible that new treatments such as coronary artery bypass grafting, PCI,  $\beta$ -blockers, lipid-lowering drugs, angiotensin-converting enzyme inhibitors and aspirin have changed the epidemiology of CAD. When a cardiac arrest occurs today, many patients might have reached an end-stage heart disease that might more frequently be reflected in asystole rather than ventricular fibrillation as the first recorded rhythm. The same trend was seen by Polentini et al. [57] and Cobb et al. [54] in the USA and earlier also by Bunch et al.[58], who speculated that the increased use of implantable cardioverter-defibrillators

(ICDs) was associated with a lower incidence of ventricular fibrillation. It is also possible that  $\beta$ -blockers themselves can contribute to a lower ventricular fibrillation frequency as a result of their pharmacological effect. Bourque et al. speculate that  $\beta$ -blockers can be used for shock-refractory ventricular fibrillation, but larger human studies are needed[59].

The decrease in ventricular fibrillation must therefore be regarded as being of multifactorial origin. However, it is important to stress that the decrease in ventricular fibrillation was mainly seen in the 1990's and, during the last decade, the occurrence of VF has remained relatively static in the whole of Sweden[2].

## **Was there a change in age?**

The median age for patients suffering an OHCA arrest in Gothenburg increased from 68 years in 1981 to 73 years in 1997[60]. With this comes the probability of a higher degree of co-morbidity, influencing both the occurrence of ventricular fibrillation and survival in a negative way[61-62]. In a later survey covering the same population, but stratified into two groups; 1980 – 2002 and 2003 – 2006, there was no significant difference in mean age between the groups[63]. Age thus appeared to increase in the early part of the 30-year follow up of OHCA in Gothenburg but not thereafter.

## **Why do we find fewer women than men in our register?**

The female coronary heart disease pattern differs from that of men. The female coronary heart problems start at a higher age and do not catch up with the male pattern over the years [64]. Since heart disease (myocardial infarction and heart failure) is the most common cause of cardiac arrest, the differences in cardiac morbidity patterns between the sexes is reflected as fewer women than men in our register. There are also other aspects to the differences in heart disease. One is that the women are more likely to be living in a nursing home because of their higher age when they suffer a cardiac arrest and are therefore not eligible for resuscitation. Another is that, with their longer life-span, an increasingly higher proportion of women are alone at a higher age and there is therefore no one to witness their cardiac arrest. As a result, they are often found too late after the collapse, when there are no reasons to start resuscitation.

# How can we explain the variability in survival over time after an OHCA?

There are a number of factors that can be part of the explanation of the variability in survival over the time period.

- Community factors – the proportion of victims who receive bystander CPR has increased dramatically, as has the percentage of crew-witnessed cardiac arrests. This could indicate better preparedness in the community, i.e. patients with warning symptoms dial 112 more rapidly and the EMS is therefore already on the scene when the patient collapses.
- EMS – there has been a major change in ambulance competence over the studied period, with a gradual increase in nurses as part of the ambulance crew. This might be reflected in a better quality of CPR, particularly chest compressions. The EMS has also been outsourced to a private contractor, which has been associated with greater occupancy of the ambulances, which has then led to a prolongation of the EMS response time.
- Mechanical chest compression – the introduction of Lucas™ could influence survival both directly and indirectly, giving the EMS staff more hands and time to perform their procedures, especially in a moving vehicle.
- Treatment factors – the decrease in ventricular fibrillation is probably an effect of the increase in the EMS response time, which affects survival in a negative way[46]. On the other hand, the percentage of survivors among patients found in ventricular fibrillation has increased over the years. A contributory factor might be the new guidelines in 2006, giving many patients with a cardiac arrest two minutes of CPR to improve the coronary flow before defibrillation, although no positive effect from this can be clearly seen when summarising all the available data[66].
- Post-resuscitation care – during the last decade, there have been major advances in post-resuscitation care, with a higher degree of PCI and the mild hypothermia treatment introduced in routine post-resuscitation care[46-53, 63]. There has also been an increase in treatment with ICD, which has been associated with improved survival[67-69].

## **Is our OHCA study population representative and how does it differ from other cardiac arrest populations?**

There is a wide variation in the populations from different cardiac arrest studies, and this becomes very clear when reporting according to the Utstein guidelines. In the case of age and gender, there is, in the literature, a spread and a tendency towards higher age and an increasing proportion of females in the studies as the years have passed. For example, the ARREST-study [70] published in 1998 reported a mean age of 64 years and 22 per cent women, Giraud et al. reported a mean age of 58 years with 26 per cent women in their survey conducted in 1991-1992[71], the mean age was 67 years and there were 30 per cent women in Böttiger's survey from Heidelberg conducted in 1992-1994[72], while the ROC Epistry – Cardiac arrest study [73] published in 2011 had a median age between the different centres involved of 64 years to 71 years and 30 – 44 per cent women. Our population, as described in the fourth article [74] published in 2010, had a mean age of 68 years and a median of 72 years, with 32 per cent women. As shown in the thesis[75], the time intervals from call received to EMS arrival at the scene also have a wide range between different studies[20, 70-71, 73, 76-77], ranging from four to thirteen minutes (median). In our setting, we reported five minutes. There is also a wide spread of the proportion receiving CPR after a cardiac arrest, ranging from 21 per cent to 60 per cent [20, 70-71, 73, 76-77]; we reported 27 per cent.

We conducted a validation study in 2009 and found that ten percent of all OHCA cases were not reported to the register and that we thus collected data from 90 percent of all OHCAs[78]. We therefore find it appropriate to assume a relatively high degree of representativeness in our OHCA population.

## **Is our OHCA population comparable to that in other parts of Sweden?**

In fact, regional differences in term of survival, delay time and bystander CPR have been found to be relatively small[79]. However, over the years survival after OHCA has been slightly higher than in the rest of Sweden. In spite of this, there are regions where survival is very similar to that in Gothenburg (in 2011 even higher).

## **Can we rely on our time measurements?**

The time measurement is a critical part of all cardiac arrest investigations. Kaye et al. investigated the time measurement for IHCA using the National Registry of Cardiopulmonary Resuscitation (NRCPR) launched by the American Heart Association and found that the data for time intervals were missing in 11 per cent of the interventions and negative intervals were calculated for four per cent of the interventions[80].

At Sahlgrenska University Hospital, the nurse at the scene measures the delay between the call and the start of various treatments using only one clock to avoid inter-clock differences. The times are noted in the nurse's cardiac arrest report. However, the accuracy of the time measurements has never been carefully evaluated. There are of course particular problems when IHCA occurs outside regular wards.

The time measurement in the OHCA setting is a difficult procedure. In 2004, there was a major change in the way the time frame for the event was collected. Prior to 2004, the EMS crew asked the witnesses about the time of arrest and when the call to the EDC was made. They then added the times measured by themselves at the scene to obtain the whole time frame for the event. After 2004, a computerised system was introduced; it keeps track of all the times from the call received by the EDC to the point when the ambulance arrives at the scene. To avoid inter-clock differences in the OHCA setting, all time intervals are taken from a single clock once the ambulance is at the scene.

As with IHCA, our studies suffer from the lack of a careful evaluation of the appropriateness of our time measurements.

## **What is the impact of the introduction of mechanical chest compression in our EMS system?**

We assume that the introduction of mechanical chest compression has been a benefit for the EMS crew, making their job easier when performing CPR during transportation and giving them time to focus on other practical matters in resuscitation. Perhaps the safety aspect is even more important when performing CPR during transportation.

However, we have not been able to verify that the introduction of the mechanical chest-compression device has influenced survival, since many important factors have been altered during the successive implementation of the device in our system. This is in line with the recently published Cochrane review of the subject of mechanical chest-compression devices versus manual CPR [81], indicating no evidence of increased survival with the device. Two large randomised studies comparing the two treatment alternatives will soon be published. We also need to know more about the risk of harm (autopsy studies).

## **Is it appropriate to divide patients who suffer from cardiac arrest into in-hospital and out-of-hospital cardiac arrest?**

The two scenes, inside and outside the hospital, differ very much in terms of organization and outcome. The IHCA setting has many advantages, with a very high degree of witnessing, a rapid start of CPR by a professional and rapid defibrillation. The ICU and post-resuscitation care is also much easier and faster to access for IHCA cases, giving them the best chance of survival. This is clearly shown in survival and time intervals when compared with the situation out of hospital, as in the fourth article. They are also two different organisations, which make them more difficult to hold together in a scientific programme. Our studies in Gothenburg have the "smaller city advantage", i.e. there is one EMS service and a limited number of hospitals for the EMS to bring the OHCA cases to. This is much more difficult in a large city with several EMS services and hospitals.

It is reasonable to assume that the in-hospital population has more severe comorbidity. However, no study that have carefully have addressed these issues is available. The DNAR issues differ completely between OHCA and IHCA. Patients with an IHCA have a known disease in the vast majority of cases and, furthermore, their psychosocial situation is well known. These facts facilitate the DNAR decision. It is different in OHCA. In this case, previous history and psychosocial factors are mostly unknown. The above-mentioned reasons make it reasonable to divide cardiac arrest into OHCA and IHCA. The importance of studying IHCA and OHCA separately is also supported by Moler et al. for paediatric cardiac arrest[82]; they conclude that the IHCA and OHCA populations differ greatly and require independent clinical trials.

## **Which are the most prominent differences between these two groups in terms of patient outcome, treatment and characteristics?**

In our material, we can see that survival is about five times higher for IHCA than for OHCA. If a comparison is made between some major studies of IHCA[5, 83-87] a mean survival of about 20 per cent is found. Some major studies of OHCA show a mean survival to discharge rate of about seven per cent[19-20, 70-72, 76-77, 88-94] which suggests three times better survival after IHCA than OHCA.

The most prominent differences in treatment between the two groups are delay to treatment, with the call for a rescue team being made three times as fast in hospital, time to the arrival of the rescue team being more than twice as fast inside the hospital and the time to defibrillation being ten times longer for the OHCA setting. Another major and important difference was the higher proportion of ventricular fibrillation after IHCA. One major contributory factor to this finding is most probably a shorter time between collapse and first ECG recording in IHCA.

## **Why is survival so different between the two groups?**

The two scenes, inside and outside hospital, differ very much in terms of organisation and structure.

The in-hospital cardiac arrest setting has many advantages, with a very high degree of witnessing and a quick start of CPR by a health care professional. The quality of CPR is important for survival [95] and can be presumed to be better within hospital and thereby affect survival positively. The proportion of patients found in ventricular fibrillation as the first recorded rhythm declines with every minute that passes after the collapse. The high degree of witnessing leads to rapid defibrillation after IHCA. This leads to high survival and, if it is very rapidly performed, very high survival [96] after IHCA, as shown in the third article of the thesis. The ICU and post-resuscitation care is also much easier and access is faster for IHCA cases, giving them the best of chance of survival.

However, there are still questions which remain unanswered. Why did the place of cardiac arrest remain as an independent predictor even after adjustment for delay to defibrillation? There must be other factors involved that we were not able to isolate.

Another important question that remains unanswered was why survival was seven times higher when cardiac arrest presenting as non-shockable rhythm took place in hospital as compared with outside hospital. Possible contributory factors to the latter two issues are quality of CPR and perhaps also an early start of ACLS, although the evidence in favour of the latter two is limited[97, 98]

## **Why did we find such a high survival after IHCA in our hospital?**

A combination of factors can contribute to this. We report a very high percentage of patients found in ventricular fibrillation, which is linked to high survival. We also report on functional Do Not Attempt Resuscitation (DNAR), thereby only starting resuscitation only in a very small proportion of patients with cardiac arrest. However, we still lack a large survey showing the variability of DNAR between different hospitals. The fact that we have a dedicated emergency medical team on call at the hospital around the clock might be an important factor, which has been recently shown to influence survival[99]. The team consists of a cardiologist, an internal medicine specialist and an anaesthesiologist. This gives the team a high competence level. The hospital also conducts CPR training on a regular basis for all hospital staff groups and has easily accessible defibrillators on every floor where any form of patient care is carried out. We cannot exclude the possibility that, over the years, dedicated persons (local champions) have stimulated the ward staff to do a good job.

A comparative study has been conducted of ward staff at Sahlgrenska University Hospital and ward staff at hospitals in Finland. The aim was to evaluate the skilfulness of hospital staff in an artificial cardiac arrest[100] and it revealed better defibrillator skills and resuscitation techniques among the Sahlgrenska ward staff.

Another important factor is the place of IHCA. At Sahlgrenska Hospital some IHCA's occur in the cath lab where the chances of survival have been reported to be better[2] or at the ICU or at the CCU where the survival also have been reported to be higher[101].

## **Are our IHCA patients representative of those in whom CPR was started?**

We have checked the reported cases with the lists from the switchboard and retrospectively reported missing cases.

However, there is one group we cannot control and that is patients who have ventricular fibrillation and are successfully defibrillated without calling for the rescue team. If these patients were reported, the results might improve even further.

## **Is it possible to improve survival after IHCA even further?**

We are chasing smaller and smaller proportions of survivors from various diseases and, to accomplish this, we need more and more resources. Although this is a problem for many parts of medicine, the reality is often driven by cost-benefit analyses. We pointed out the very high survival [96] in the third article for patients who were defibrillated within three minutes, regardless of monitoring facilities on the ward. Efforts could be made to reach even more patients with a shockable rhythm within three minutes.

Future candidates for improvement could also be patients found in non-shockable rhythms, which have very low survival today. Even more rapid treatment of these patients might perhaps improve survival even further. We finally believe that the quality of CPR can improve still further with a corresponding further increase in survival. In the distant future it is also possible to imagine an artificial heart which would to improve the long-term survival and portable Extra-Corporeal Membrane Oxygenation (ECMO)[102] might also play a role here.

## **Should we accept that patients are defibrillated later than three minutes after in-hospital ventricular fibrillation in the future?**

It is very clear that, the faster the defibrillation is performed, the higher the survival. It is also clear that survival decreases quickly with delayed defibrillation; every minute counts. We also have shown that survival on non-

monitored wards is twice as high for patients found in shockable rhythms if defibrillation is performed within three minutes of the collapse as compared with delayed defibrillation.

Today, at Sahlgrenska University Hospital, a “deviation report” should be written if patients who are found in ventricular fibrillation are defibrillated later than three minutes after collapse. It can be assumed that, if all patients in Sweden with IHCA found in ventricular fibrillation were defibrillated within three minutes after collapse, a large number of lives could be saved.

## **How soon should patients be defibrillated after OHCA in the future?**

With increasingly improved prophylactic medicine, increased knowledge in the general population about lifestyle impact on health, improved medical treatment for cardiac conditions and earlier discovery of early signs of cardiac problems, the saying “hearts too good to die” [103] might hopefully be diminishing.

In their recently published study, O’Keeffe et al. [45] stated that the cost of reducing the EMS response times after a cardiac arrest by one minute was estimated at around 54 million pounds sterling (about 586 million SEK in September 2011). This is for a British setting, so the amount is not necessarily the same in Sweden, but it illustrates the large sums that are required to shorten response times.

For all cardiac arrest cases, the phrase “less is more” is a very powerful truth when it comes to the time of intervention and the time between the links in the chain of survival. In Gothenburg the time intervals have increased over the years. This must change. The Swedish resuscitation council has set a goal i.e. patients found in ventricular fibrillation should be defibrillated within five minutes after collapse. This is an ambitious goal which requires the support of the community (AEDs used by lay persons, firebrigade, policemen and so on). This is a process that is developing rapidly in Sweden. Today there are about 3200 AEDs[104] in use outside the EMS system. In many communities, collaboration already exists between the EMS and the fire brigade. Examples include Stockholm, Södermanland and parts of Västra Götaland.

## **Why does it appear that cerebral function was better among survivors after IHCA than after OHCA?**

We do not have data on the prior condition for OHCA patients. Is it possible that they have a different CPC pattern before the cardiac arrest than the IHCA patient group? We think this is unlikely. There are reasons to assume that the substantially shorter time intervals to treatment after IHCA should reduce the period of impaired cerebral blood flow, thereby minimising the brain injury.

However, there is good news. Recent data from the Swedish Cardiac Arrest Register suggest that the CPC score among survivors of OHCA is relatively similar to the CPC scores among survivors of IHCA[2].

Martinell et al. [63] showed that improved post-resuscitation care has gradually been implemented in Gothenburg with the increased use of coronary angiography, coronary revascularisation, and therapeutic hypothermia. This has been associated with improved cerebral function among OHCA patients who survive to hospital discharge. Patients suffering IHCA have faster, easier access to post-resuscitation care, which should benefit them in terms of cerebral outcome. However, experience from Sweden indicates that very few patients suffering from IHCA are treated with therapeutic hypothermia. A shorter “no perfusion time” is therefore most probably the most important factor behind our observation.

## **Is CPC score a representative measurement of cerebral function?**

The CPC is the preferred way of reporting neurological and cognitive outcome after cardiac arrest[9]. The advantages pointed out in the Utstein guidelines are that the outcome categories are reliable and easy to obtain, simple and practical to use, especially when compared with more elaborate interview and physical assessment methods.

The CPC is not validated, which is a problem. The CPC score did not correlate with subjective experience of quality of life, when Hsu et al.[105] tested CPC against a validated test. They concluded: “The CPC score, relied on as a measure of functional outcome in cardiac arrest, correlates poorly with subsequent subjective quality of life and with validated objective functional testing instruments, and conclusions based on it are suspect.” Rittenberger et al.[106] conclude that a more nuanced outcome measurement

specifically designed for the post-cardiac arrest population, is needed. After an ischemic brain injury, there is also relatively large healing potential and slow adjustment and adaptation to the new limitations experienced by the cardiac arrest victim. It is therefore important to measure the cerebral outcome again after six months. Arrich et al.[107] found a significant change in functional outcome (and mortality) between one and six months after cardiac arrest. It has also been shown that CPC produces an inter- and intra-reviewer variability when the same cases were interpreted by three different persons to classify favourable versus unfavourable outcome from OHCA when found in ventricular fibrillation[108].

## **How many lives are saved from a sudden cardiac arrest in Sweden today?**

In Sweden, we have a National Cardiac Arrest Registry. From this, we can extract data that show that there are about 5000 cardiac arrests in an out-of-hospital setting and approximately 3600 cardiac arrests in hospital where resuscitation is started. From these data we can extrapolate that about 500 persons are saved from an OHCA and about 900 persons are saved from an IHCA.

In all, we estimate that about 1400 persons survive a sudden cardiac arrest and the large majority with a good cerebral outcome according to CPC score[2].

## **How many lives will be saved from a sudden cardiac arrest in Sweden and Gothenburg in 2021?**

The following text is based on calculations from the Swedish Cardiac Arrest Register. For the OHCA setting, the survival to one month for patients where the call for ambulance was made within two minutes after collapse was 14 per cent. If the delay was longer, the survival dropped to eight per cent. Based on this, it is estimated that, if all calls were made within two minutes after collapse, 69 more lives would be saved during one year in Sweden. If CPR was started within two minutes after collapse the survival to one month was 17 per cent, while CPR delayed over two minutes produced a drop in survival to six per cent. If CPR was started within two minutes after collapse in all witnessed OHCA's in Sweden an additional 149 lives could be saved. If defibrillation was performed within five to eight minutes after collapse, 46 per cent of the patients survived. If defibrillation was performed later than

eight minutes, 18 per cent survived. If all patients in the future could be defibrillated within five to eight minutes after collapse, an additional 192 lives could be saved. Based on these assumptions, it can be estimated that, with improvements in logistics with the shortening of the delay to call, the start of CPR and defibrillation, about 300 – 400 further lives could be saved after OHCA in Sweden.

In terms of IHCA, delay to treatment today is already relatively short. However, calculations from the Swedish Cardiac Arrest Register indicate that a further 150 – 200 lives could be saved by shortening the delay to call, the start of CPR and defibrillation appropriately. Today, we resuscitate almost 1500 victims of cardiac arrest to survival and, in 2021 it is to be hoped that this figure will have increased to at least 2000 if the logistics are gradually improved. In Gothenburg the corresponding increase in the number of lives saved per year would be 100 to 130 lives saved per year in 2021.

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