Rehabilitation after Resuscitation

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Chapter 1
General introduction

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Out-of-Hospital Cardiac Arrest: definition, cause and incidence

The life changing event 'out-of-hospital cardiac arrest' (OHCA) presents itself suddenly and unexpectedly. It is characterised by interruption of the blood circulation through the body by abnormal or no electrical activity in the heart. Between 65% and 89% of the out-of-hospital cardiac arrests are of cardiac origin and predominantly caused by coronary artery disease.[1]
It is difficult to give exact numbers for the incidence of adult OHCA worldwide. The cause of death registered via death certificate records is not always reliable.[2] Besides, death certificate records compared with autopsy reports show that 24-45% of the suspected death causes turn out to be false.
More relevant information might be collected via the registration of emergency medical services, since they treat the patients that may survive the OHCA. However, the availability of emergency medical services varies greatly throughout the world due to differences in health care system, gross national product, infrastructure and population density.[3] Despite these differences, registrations of treated OHCA by emergency medical services seem to yield the most reliable data so far. Using this data shows that in four regions in the world (Europe, Eastern Europe, North America and Australia) the incidence of emergency medical service (EMS) attended OHCA ranges from 52.5 to 112.9 per 100.000 person years [Fig. 1]. [3] For the continents South-America and

Fig. 1 Incidence four regions of the world EMS-attended OHCA (100,000 person-years) Berdowski et. al. 2010 [3]

Africa similar data are not available. Specifically in the Netherlands, the incidence of EMS-treated OHCA is approximately 37/100.000 person years.[4]

With respect to the situation after arrival in a hospital, the rates of survival to discharge also vary, ranging from 2% in Asia to 9% in Europe and 11% in Australia. In The Netherlands, in EMC treated OHCA the average survival rate until discharge is 23%.[5] This relatively high survival rate can be explained by the optimised network of ambulance facilities and other first responders, leading to short arrival times and thus to a relative high number of shockable rhythms. Besides, the wide availability of automatic external defibrillators (AED) is playing a positive role.[4,6]

Cardiopulmonary resuscitation – a historic overview

History shows that humankind already tries for millennials to revive people from the dead, but a successful resuscitation is difficult to achieve. In 3000 B.C. the Greeks and Egyptians already described attempts of respiration and revival techniques, like breathing air into the mouth, throwing water in the face or rectal fumigation. Since the 18th century serious attempts to resuscitate people were based on specific protocols. Abraham Calkoen, bailiff in Amstelland (Amsterdam) in 1766, encountered many people who could not swim and drowned after falling into one of the many canals in his area.[7] He developed a roadmap to make sure that no living people were buried. Then, Cornelius van Engelen was the first to make a protocol focussing on reviving drowned people.[8]

"*Men weet dat er in een Land, zo vol water als het onze, Jaarlyksch eene menigte Menschen verdrinken; maar het is minder bekend, dat de meesten dier ongelukkigen omkoomen by gebrek van eene goede behandeling, na dat zy uit het Water zyn gehaald. (…) Men geeft deze ongelukkigen ondertusschen op, zodra men ze heeft opgevischt, of men behandelt ze op eene gansch verkeerde wyze, en men stopt er van tien, welken men hadt kunnen behouden, misschien negen onbarmhartig onder de Aarde.*"

Original text from Cornelius van Engelen in De Philosooph,
24 of august 1767

In response to his suggestion the 'Stichting Maatschappij tot Redding van Drenkelingen' (Society to Rescue People from Drowning) was founded in 1767. The advice was to follow the method of the French doctor Isnard: rub the drowned person with warm cloths, stimulate the throat with a feather, put pungent substances into the mouth, try to make the victim throw up and open the intestines by blowing smoke of a tobacco pipe into the rectum and finally letting his blood.[9] Although the methods in those days were not based on a pathophysiological framework the first 'resuscitation' protocol was a fact.

Discovering heart massage

Reviving drowned people was focussed on the observation that patients did not breath anymore. In the 19th century the focus shifted from breathing towards the heart. Due to observed cardiac arrests of healthy patients when using chloroform as anaesthetics, doctors became more aware of the function of the heart.[10] This resulted in and increased interest in how to restart the heart, eventually leading to the concepts of open and closed chest cardiac massage.

The first closed chest heart massage was described in 1868 by John Hill, a surgeon from London, the United Kingdom.[11] But it was not until 1958 that the importance of closed chest massage was acknowledged when Kouwenhoven, Knickerbocker and Jude accidentally discovered chest compression. Studying defibrillation in dogs they noticed that by forcefully applying the paddles to the chest of the dog, a pulse in the femoral artery was achieved. Further research provided information about how fast, where and how deep to press.[12]

Defibrillating the heart

In parallel with the discovery of the effects of (closed) chest massage, the value of electric defibrillation of the heart was discovered. The first successful defibrillation of a patient was in 1947 by Claude Beck.[13] In that time, the defibrillator consisted of two silver paddles and was to be used in open-chest situations. William Kouwenhoven had been working since the 1920's on a closed chest (external) defibrillation machine, but Paul Zoll was in 1956 the first to publish about a transcutaneous approach to terminate ventricular fibrillation.[14] In 1966 the first "portable" defibrillator was introduced.[15] It was a heavy and rather unpractical machine, weighing 70 kilograms. This was also the year that the world's first mobile intensive care unit was equipped with a

defibrillator powered by two 12-volt car batteries. In 1968 an improved version came available with the weight of only 3.2 kilos.[16] This lighter version made it possible that trained healthcare professionals were able to defibrillate people with a cardiac arrest in- and outside the hospital.

Mouth-to-mouth resuscitation
Additional to heart massage and defibrillation breathing is an important factor in resuscitation. Elam reported in 1956 that exhaled oxygen can be used as an adequate resuscitative gas.[17] Following this, Safar and Elam reported about mouth-to-mouth breathing and the importance of the head tilted backwards during this performance.[18] They also demonstrated that mouth-to-mouth breathing could be provided by lay people.

Cardio Pulmonary Resuscitation
In 1960 the above described developments of heart massage and mouth-to-mouth breathing were combined to sustain the circulation of oxygenated blood until a defibrillator had arrived to restart the heart. The basis of the currently available Automatic External Defibrillators where trained lay persons defibrillate and perform Cardio Pulmonary Resuscitation in a wide range of places, was made.
In 1989 Mary M. Newman described four steps in the process of resuscitation in the 'chain of survival' as seen in figure 2.[19] Her aim was to optimise the different links during cardio pulmonary resuscitation in order to increase survival rates.

Fig. 2 Chain of survival by Mary M. Newman

- Early access to emergency medical care
- Early cardio pulmonary resuscitation
- Early defibrillation
- Early advanced cardiac life support

The first three links may involve lay bystanders with some basic skills, like first-aiders at work, police and fire fighters. The third link in the procedure is crucial, since defibrillation is a prerequisite to restore cardiac function. Figure 3 shows that every additional minute till defibrillation reduces chances of survival by ~10%. The fourth link in this scheme is the early advanced care, often delivered by paramedics.

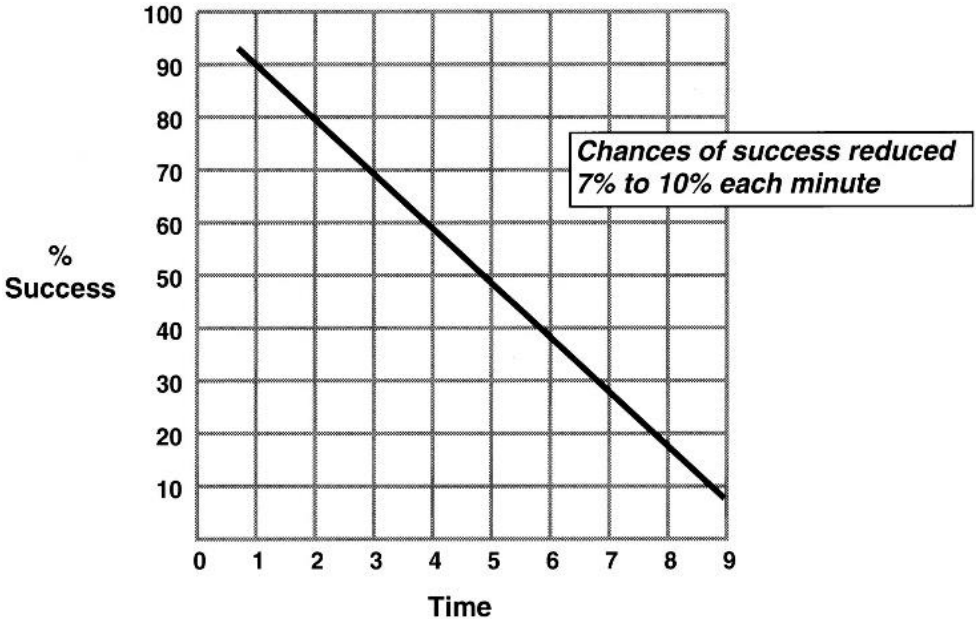

Fig. 3 Relationship between probability of survival to hospital discharge (indicated as "success") after ventricle fibrillation cardiac arrest and interval between collapse and defibrillation. Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Circulation Aug. 2000. Based on: Larsen MP et al. Ann Emerg Med. 1993;22:1652–1658.

In 2016, the chain of survival was updated by Eisenberg et al. [Fig. 4]. [20] More attention was paid towards the interaction between bystander and dispatcher and more focus was laid on the post resuscitation care.

- Call for help and start cardio pulmonary resuscitation
- Dispatcher activates resources and coaches cardio pulmonary resuscitation by telephone
- First responder provides high-performance cardio pulmonary resuscitation and defibrillates
- Paramedics provide advanced life support
- Post-resuscitation care in hospital which covers the emergency department, catheterisation laboratory and intensive care unit.

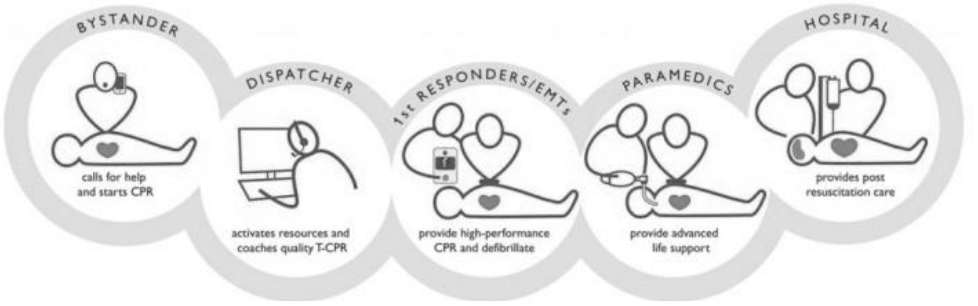

Fig. 4 Chain of survival by Eisenberg 2016

The chain of survival is strengthened by the nowadays widely available portable AED's in first responder vehicles such as police and fire brigades and in many public areas. The most recent development is the setup of networks of civilians that provide cardio pulmonary resuscitation as quick as possible. [21,22] Dispatch centres not only alarm ambulance services but also people nearby the collapsed patient receive an SMS on their mobile phone to assist with cardio pulmonary resuscitation or bringing an automatic external defibrillator. The results of involving people through a network of trained citizens (aprox.170.000 in 2017), together with the increasing numbers of AEDs throughout the country (approx. 100.000 in 2019) are very promising. [23,24] With the improvements made in the chain of survival, survival rates actually have increased in the Netherlands from 12-18% to 16-35% (population density depended) in Limburg and 33% to 47% in Nijmegen. [23,25]

In the region Leiden efforts are made to optimise the care for people suffering from an OHCA via a cooperation between the Leiden University Medical Center and the regional ambulance service 'Hollands Midden'. Positive environmental factors are the high population density (926 km^2 https://opendata.cbs.nl/statline/#/CBS/nl), with many first responders and high availability of AED's (>400), leading to short responder times (75% <6 minutes). Besides, the municipalities of Hollands-Midden put much effort in resuscitation by organising satellite ambulance posts, optimising the resuscitation protocol in the ambulance and by concentrating the acute OHCA treatment to one hospital, the Leiden University Medical Center. In what extend patients attending the hospital survive until discharge and what factors are associated with survival in the region Leiden is not known.

Successful resuscitation and consequences for the brain

Patients who get return of spontaneous circulation after OHCA may experience a sequelae of hypoxic ischemic brain injury (HIBI), possibly resulting in physical, mental and cognitive impairments. HIBI can be explained by a 'two-hit' model: primary injury during the cardiac arrest and secondary injury occurring after the resuscitation.[26] During the cardiac arrest itself, the primary injury, cessation of oxygen occurs resulting in neuron ischemia and cell death within minutes causing substantial neuronal loss. In the hours and days following the initial cardiac arrest secondary injury is playing a major role in the aetiology of brain injury. Factors causing this secondary injury include ongoing ischemia, reperfusion injury, microcirculatory dysfunction, impaired cerebral autoregulation, hypoxemia, hyperoxia, hyperthermia, fluctuations in arterial carbon dioxide, and concomitant anaemia. The pathophysiology of HIBI causing all these problems is very complex. [27]

The best chances of preventing HIBI are probably inherent to the Cardio Pulmonary Resuscitation: quickly restoring circulation and oxygenation in order to avoid deoxygenation of the brain and thereby also minimizing the secondary sequela. Immediate availability of an AED is probably most important, since the chance of a shockable rhythm is the highest in the first minutes after cardiac arrest. [28,29]

During hospital stay several interventions are undertaken to prevent secondary injury. Prevention of post-cardiac arrest fever by targeted temperature management seems to reduce mortality and brain damage. [30] However, the exact mechanisms for this targeted temperature management are not clear yet. [30,31,32] Early coronary revascularisation, aiming at restoring oxygenation of the heart and consequently improving circulation of the body and brain, can also be seen as a measure to prevent the second hit. Both percutaneous coronary intervention, treating stenosis of coronary arteries, and coronary artery bypass grafting can be carried out for this goal.
Despite these interventions, brain injury is still a major and common problem in survivors after an OHCA. Approximately 42-50% of the survivors after an OHCA experience cognitive problems. [33] Unfortunately cognitive impairments, especially when they are mild, are not always detected by others, but may have a big impact on a person's life and his or her family. [34]

To describe the functional outcome of patients after an OHCA the Cerebral Performance Category (CPC) is recommended by the Utstein-style guidelines [Fig. 5].[35] The CPC is a short observational instrument distinguishing 5 categories. The lower the score the better the outcome. CPC scores of 1 and 2 are mostly considered as 'good' outcomes and CPC scores of 3, 4 and 5 as 'poor' outcomes. [36]

CPC1	Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychologic deficit.
CPC2	Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
CPC3	Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
CPC4	Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.
CPC5	Brain death: apnea, areflexia, EEG silence, etc.

Note: If patient is anesthetized, paralyzed, or intubated, use "as is" clinical conditions to calculate scores.

Safar P. Resuscitation after Brain Ischemia in Grenvik A and Safar P Eds: Brain failure and Resuscitation, Churchill Livingstone, New York, 1981; 155-184.

Fig. 5 Cerebral Performance Categories Scale CPC Scale

All patients with a 'good' outcome of a CPC 2 do experience cognitive problems but can function independently when doing simple tasks like getting dressed and housekeeping. Patients with a CPC 1 are indicated as having a good cerebral outcome and are even able to work again. But unfortunately a considerable proportion (15-52%) of this group does experience cognitive problems that are not noticed by the CPC Scale. [37,38] A good outcome in the CPC is therefore rather relative and does not imply good functioning in daily life. What is needed is a sensitive screening for all survivors of an OHCA.

Identifying cognitive problems after OHCA

In the last 20 years the interest in cognitive problems after an OHCA is increasing. The first study that recommends assessment of memory function as a standard part of post discharge management after an OHCA dates from 1997. [39] Approximately ten years later, this recommendation found its way to the European guidelines in 2007 and to the Dutch guidelines in 2011. [40]
The rates of 42-50% of OHCA-survivors who have cognitive impairments were found in studies using sensitive neuropsychological tests to assess cognitive functioning in all OHCA survivors. These tests are specifically designed to measure different psychological functions and are linked to particular brain structure(s) or pathway(s).[41] Neuropsychological tests are a core of any neuropsychological assessment, along with tests covering personal, interpersonal and contextual factors. However, neuropsychological testing requires highly trained staff and is very time consuming as it takes approximately 1,5 hours. As a consequence, this procedure may require referral to specialised departments and is not practical as a first screening.

Cardiac rehabilitation after OHCA

According to the Dutch Multidisciplinary guidelines of cardiac rehabilitation all patients after an OHCA with a cardiac cause are eligible for cardiac rehabilitation.[40] Cardiac rehabilitation programs in the Netherlands focus on physical activity, health education and stress management to improve exercise capacity, quality of life and psychosocial wellbeing.[42] Another positive effect is reduction of mortality, morbidity and unplanned hospital admission. The final goal is that the patient can return to normal life and keep up with the lifestyle changes. The cardiologist of the hospital is responsible for referral to an adequate cardiac rehabilitation program. Common cardiac rehabilitation, supervised by a cardiologist, is a 6-week program offered in the hospital to low risk patients. Complex cardiac rehabilitation, supervised by a rehabilitation specialist or specialised cardiologist, is available for high risk patients who have multiple demands of care that needs to be treated on an individualised base. In these complex programs, exercise training and education about life style changes are mainly given in groups and individual counselling is provided on depression, fear, social interactions and sexual impairments. Complex cardiac rehabilitation takes on average 8 to12 weeks.

When OHCA patients are referred to non-complex cardiac rehabilitation, in the best case a psychologist and social worker are involved in group sessions, but no one pays specific attention to possible cognitive complaints or burden of the care givers. But also after referral to complex cardiac rehabilitation, the focus of the cardiac team is on social aspects, fear and depression without paying attention to possible cognitive problems. Probably, mild cognitive impairments are not recognised by referring cardiologists and most cardiac rehabilitation teams.[33] Therefore it is important that cardiac rehabilitation not only focusses on physical and emotional problems, but also on timely recognition of cognitive problems, so that adequate referral can take place if needed.

Cognitive rehabilitation after OHCA in the Netherlands?

In the Netherlands, patients with participation problems due to cognitive problems caused by brain injury are eligible for cognitive rehabilitation. In facilities for specialised medical rehabilitation, a rehabilitation specialist inventories the functional prognosis of the patient and assesses which modalities are treatable through rehabilitation. Thereafter the rehabilitation specialist will determine, together with the patient, what the main problems are and which goals are set for the cognitive rehabilitation. The patient will follow a (mainly) individual program set up by a multidisciplinary team. The period of a cognitive rehabilitation program depends on several factors and varies between 6 weeks and 6 months. Cognitive rehabilitation focusses mainly on the effects of the cognitive impairments on 'activity and participation' based on the International Classification of Functioning, Disability, and Health (ICF) of the World Health Organization [Fig. 6].[43] This framework reports health consequences of a disease or disorder on an individual base across all domains of functioning in daily life.

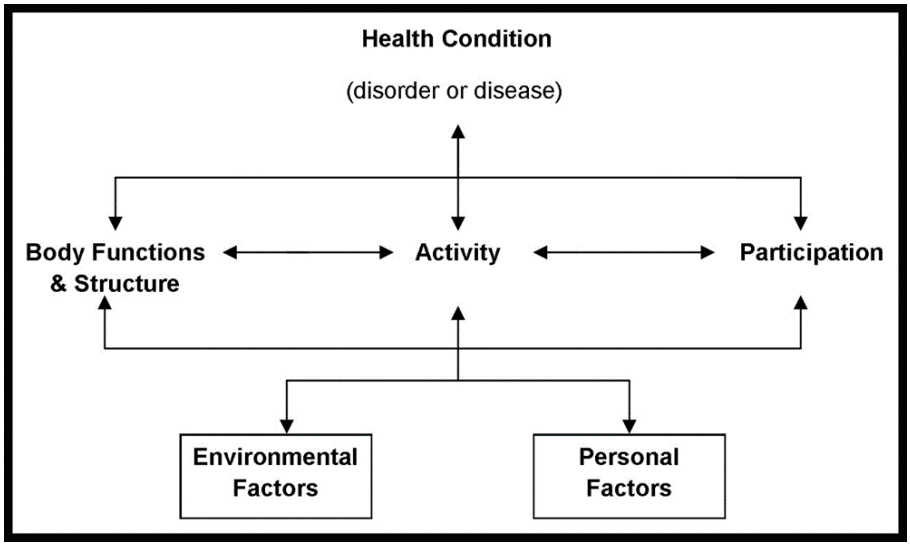

Fig. 6 International Classification of Functioning, Disability and Health (ICF model) WHO [43]

The cognitive rehabilitation exists of teaching strategies or compensation techniques that enable patients and their families to live with, manage, by-pass, reduce or come to terms with cognitive deficits.[44,45] Due to the specific knowledge of the teams working in the field of cognitive impairments, most often the knowledge on other domains, among which is knowledge on cardiac exercise capacity, is limited. In order to fulfil this gap of knowledge professionals involved in cognitive rehabilitation need to know how to integrate limited cardiac exercise capacity in a cognitive rehabilitation program.

Integrated care

The goal of rehabilitation after a cardiac arrest is to provide patient-centred cardiac and cognitive rehabilitation to patients and their spouses in order to achieve optimal participation in society, with minimal burden for spouses and society. So far, no care path is available where cardiac and cognitive rehabilitation is coordinated in an integrated care path.

General aims and outline of this thesis

The general aim of this thesis is to contribute to the knowledge of rehabilitation treatment after OHCA, so that all patients that survive an OHCA get the treatment they need at the right time and the right place. For this purposes, this thesis addresses a number of knowledge gaps:

I Evaluation of survival of OHCA-patients treated by the emergency medical service in current daily practice and factors associated with survival.
II In what extend do OHCA survivors referred for cardiac rehabilitation experience cognitive problems and what screening tool can be used to assess these possible cognitive problems. Also the effect of cognitive problems on the exercise capacity is described.
III Comprehensive description of rehabilitation treatment by integrating cognitive and cardiac rehabilitation in one care pathway and the point of view on this of healthcare providers.

The first part of this thesis, chapter 2 to 4, describes the characteristics of the OHCA-patients and OHCA survivors attending cardiac rehabilitation program

Chapter 2 describes the survival rates in hospital after an OHCA in an optimised chain of survival in the region Leiden.
Chapter 3 describes the presence of cognitive complaints in patients referred for cardiac rehabilitation after an OHCA using a concise screening.
Chapter 4 concerns a study that determines whether there are differences in exercise capacity between Myocardial Infarction induced OHCA survivors with and without cognitive impairments. The results of this study are relevant for the design of rehabilitation programs after an OHCA.

The second part of this thesis describes aspects of the rehabilitation treatment for OHCA-survivors.

Chapter 5 describes the content of a best practice, a care pathway for survivors of an OHCA 'Rehabilitation after Resuscitation' where cardiac and cognitive rehabilitation are integrated.
Chapter 6 presents the results of a study on the uptake of the recommendations regarding cognitive screening and rehabilitation in OHCA-survivors as described in literature and recent guidelines. Additionally barriers and facilitators that influence the uptake of these recommendations for OHCA-survivors are described. Insight in the uptake of these recommendations is needed to enhance future initiatives that aim to improve the quality of care delivered to OHCA-survivors.
Chapter 7 an overview of recent developments in the field of rehabilitation for OHCA-survivors is given.
Chapter 8 Summary and general discussion.
Chapter 9 Summary of this thesis in Dutch.

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