Rehabilitation after Resuscitation

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Content of this thesis

Chapter 1
General introduction

General introduction

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.

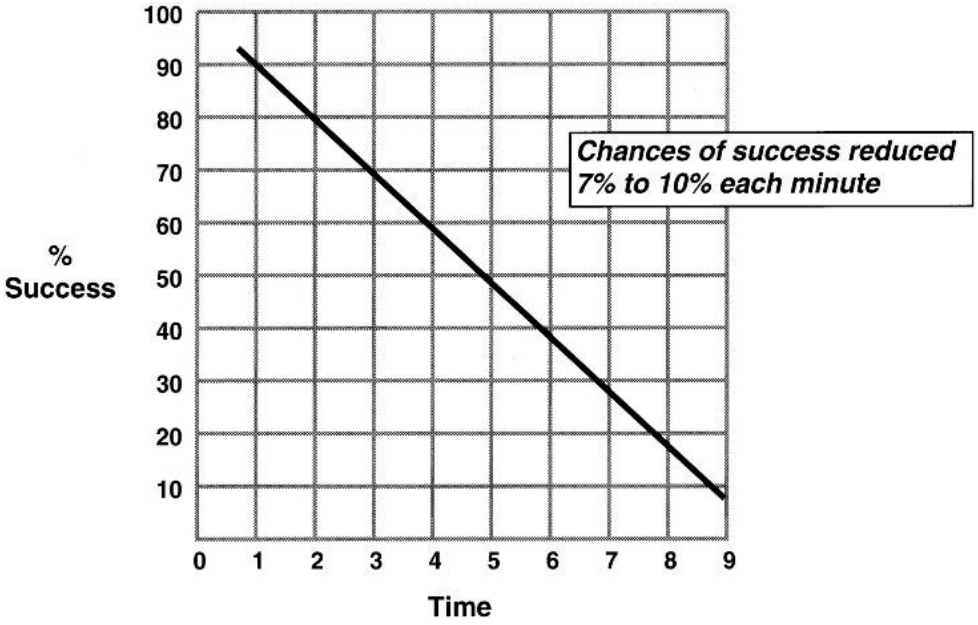

Fig. 3 Relationship between probability of survival to hospital discharge (indicated as "success") after ventricle fibrillation cardiac arrest and interval between collapse and defibrillation. Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Circulation Aug. 2000. Based 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.

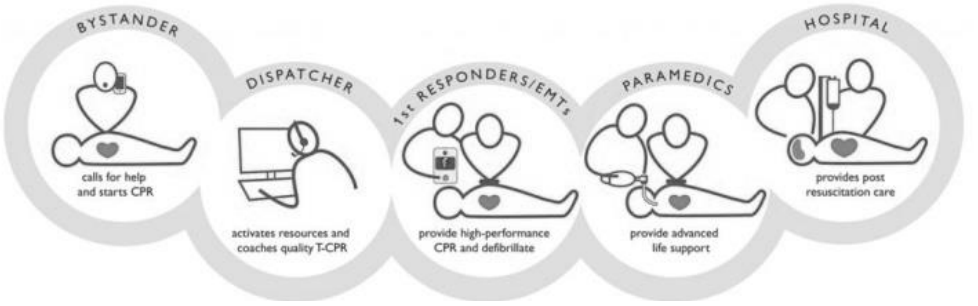

Fig. 4 Chain of survival by Eisenberg 2016

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.

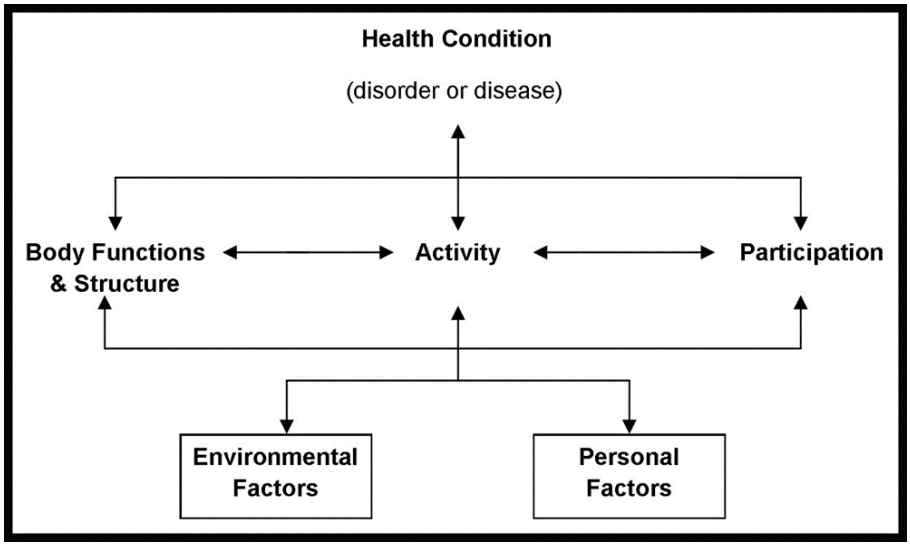

Fig. 6 International Classification of Functioning, Disability and Health (ICF model) WHO [43]

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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Chapter 2

High survival rate of 43% in out-of-hospital cardiac arrest patients in an optimised chain of survival

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Abstract

Aims
Survival to hospital discharge after out-of-hospital cardiac arrest (OHCA) varies widely. This study describes short-term survival after OHCA in a region with an extensive care path.

Methods
Consecutive patients ≥16 years admitted to the emergency department between April 2011 and December 2012 were included. Socio-demographic data, characteristics of the OHCA and interventions were described and associations with survival were determined.

Results
242 patients were included (73% male, median age 65 years). In 76% the cardiac arrest (CA) was of cardiac origin and 52% had a shockable rhythm. In 74% the CA was witnessed, 76% received bystander Cardio Pulmonary Resuscitation and in 39% an Automatic External Defibrillator (AED) was used. Of the 168 hospitalised patients, 144 underwent therapeutic procedures. Until hospital discharge 105 patients survived. Younger age, CA in public area, witnessed CA, cardiac origin with shockable rhythm, the use of an AED, shorter time until return of spontaneous circulation, Glasgow Coma Scale (GCS) ≥13 during transport and longer length of hospital stay were associated with survival.

Conclusion
A survival rate of 43% after OHCA is achievable. Witnessed CA, cardiac cause of CA, initial cardiac rhythm and GCS ≥13 are associated with higher survival.

Introduction

Out-of-hospital cardiac arrest (OHCA) is one of the main causes of death in Europe. A systematic review including 67 peer reviewed studies published from 1990 to 2008 concludes that the incidence of emergency medical service (EMS) attended OHCA in Europe is 86.4 per 100.000 inhabitants per year.[1] That review also reports that 60% of the patients in Europe are treated by EMS after OHCA and 9% of these patients survive to hospital discharge. In The Netherlands survival rates seem to be relatively high: a study on EMS attended OHCA between 2005-2008 reported a survival rate until discharge of 14%.[2] In 1998, a survival rate of 36% of EMS attended OHCA was found in the Amsterdam region.[3] However, that study only included patients who had had an OHCA due to a primary cardiac cause.

Factors positively associated with short term survival after OHCA described in two systematic reviews are: younger age, male gender, witnessed OHCA, early start of cardiopulmonary resuscitation (CPR), initial rhythm of ventricular fibrillation (VF), the use of an automatic external defibrillator (AED), short time until arrival of ambulance, no EMS intubation and short time until return of spontaneous circulation (ROSC).[4,5] In-hospital factors important for survival include therapeutic hypothermia and the availability for acute cardiac interventions 24/7.[6] Revascularisation procedures and the use of an implantable cardioverter defibrillator (ICD) mainly reduce long-term mortality.[7]

In the Leiden region efforts are taken to provide an optimal chain for OHCA patients, including optimisation of acute care, treatment during transport, treatment in hospital and cardiac rehabilitation. This study aims to describe hospital survival in an optimised chain for OHCA patients.

Methods

In the Leiden area post-cardiac arrest care is organized around one regional cardiac centre (The Leiden University Medical Center, LUMC), where cardiac procedures can be performed 24/7. This centre has an affiliated area of 540km2 with 542.000 inhabitants. [Statistics Netherlands 2012, www.cbs.nl]. The 112 emergency service alarms the regional ambulance service and other first responders with all being equipped with an AED and trained personnel.
Chest compressions executed by the ambulance service are standardised using the Lund University Cardiac Arrest System (LUCASTM, Jolife AB/Physio-Control Lund, Sweden). The ambulance service transports patients to the emergency department (ED) of the LUMC (approximately 70% of the cases; personal communication). If ROSC is achieved, patients are transported to the coronary care unit (CCU) or intensive care unit (ICU). In accordance with guidelines, eligible patients receive mild hypothermia.

In the present, retrospective study patients ≥16 years, resuscitated outside the hospital and admitted to the ED of the LUMC (April 2011-January 2013) were included. Eligible patients were identified using the electronic diagnosis registry of the LUMC. To ensure no patients were missed, patient selection was checked with the registries of the ambulance service. Patients were excluded if the ambulance service decided not to transport the patient to the ED, if the collapse was not caused by CA or when insufficient information could be retrieved from the medical records.

Data were retrieved using a standardised form. A second researcher checked the data of 10% randomly selected patients. No major differences were found. The following data were extracted from the medical records: Socio-demographic data (gender and age at time of the CA); Characteristics of the CA (cause, location of CA, witnessed or not, bystanders CPR and use of AED); Treatment and course (The number of shocks provided by EMS, the initial cardiac rhythm and the interval between collapse and ROSC; The Glasgow Coma Scale (GCS) during ambulance transport or if not available at arrival at ED; (Sub) acute treatment in the hospital, number of days in hospital, hospital survival and discharge destination).

All statistical analyses were performed using the SPSS 19 software package. Descriptive statistics were used for the characteristics of the participants. Characteristics of survivors and non-survivors were compared by unpaired t-tests (Mann-Whitney U test) or Chi Square tests, where appropriate. Factors associated with survival ($p<0.05$) were entered into bivariate and multivariate logistic regression analyses, with survival until hospital discharge as dependent variable. By backward elimination, variables that lacked independent association were removed.
This retrospective study (chart review only) falls outside the remit of the Dutch Medical Research Involving Human Beings Act (Medical Ethical Review Board of the LUMC).

Results

Patients
In the study period 263 patients were identified. After examination of the medical records 21 patients were excluded. (Fig 1)
Table 1 shows the socio-demographic characteristics, characteristics of the medical condition and treatment and course of the 242 included patients. Their median age was 65 years (range 20-95) and 73% were male. 67% of the OHCAs were witnessed by bystanders and 9% by EMS personnel. 76% of the patients received bystander CPR and in nearly 40% an AED was used. Most of the arrests took place at home. The majority of the CAs were of cardiac origin with a shockable rhythm in about half of all patients at EMS arrival.

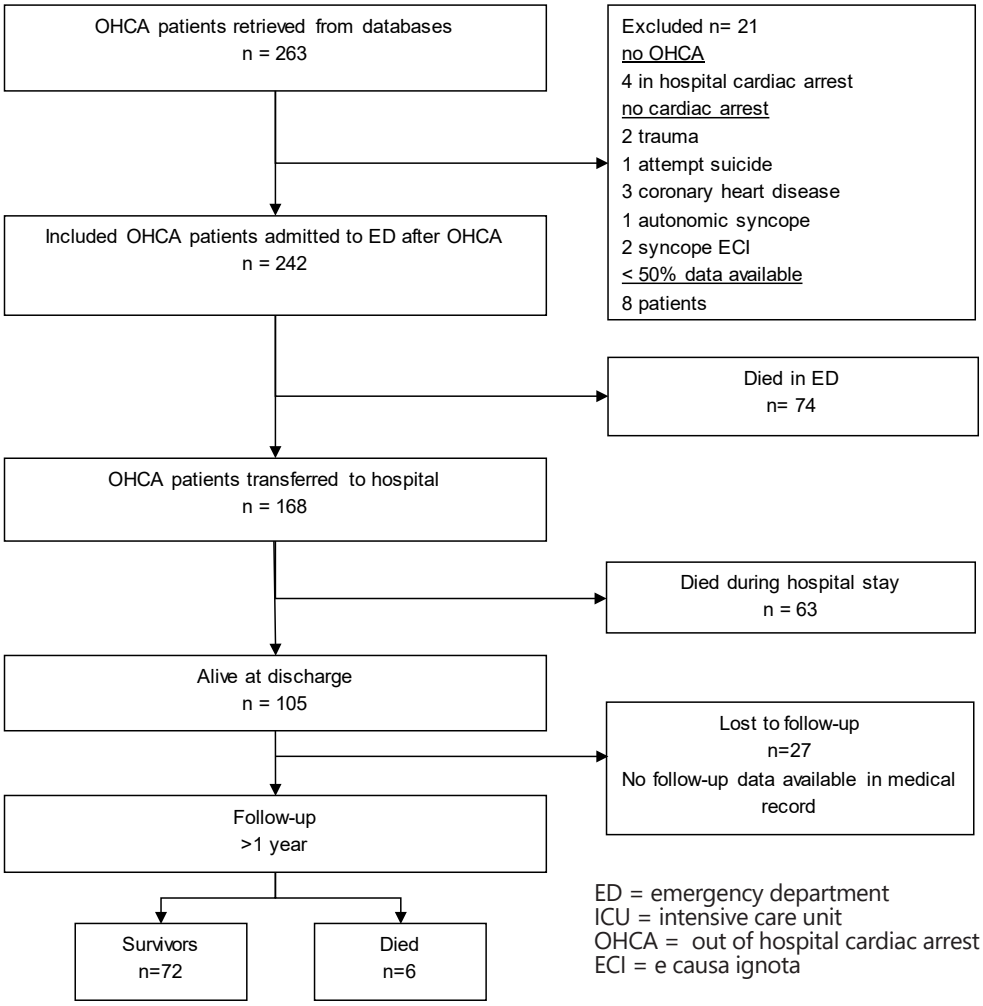

Figure 1 Flow chart of patients after OHCA

Survival and discharge destination

Of the 242 patients who attended the ED, 74 (31%) died on the emergency ward. Four of the ED stabilised patients were immediately transferred to another hospital. Of the remaining 164 patients, 63 patients died in hospital, on average 2 days after OHCA. After stabilisation on the CCU/ICU 35 patients were transferred to another hospital. In total 105 patients (43%) survived to hospital discharge. Their hospital stay was on average 9 days.

Table 1 Characteristics of 242 patients who survived out-of-hospital cardiac arrest

	All patients n=242		Survivors n=105 (43%)		Non survivors n=137 (57%)		P value[a]
	n		n		n		
Age in years, mean (SD)		64.8 (14.7)		61.5 (13.7)		67.4 (15)	.002
Male gender , n (%)		176 (73)		77 (73)		99 (72)	.853
Location of CA, n (%)							
In/around Home	241	148 (61)	105	47 (45)	136	101 (74)	<.001
Public area		93 (39)		58 (55)		35 (26)	<.001
Cause CA, n (%)							
Cardiac	240	183 (76)	104	93 (89)	136	90 (66)	<.001
Non-cardiac		57 (24)		11 (11)		46 (34)	<.001
Witnessed CA, n (%)							
Yes	237	159 (67)	103	82 (80)	134	77 (57)	<.001
CPR, n (%)							
CPR bystander	240	123 (51)	104	57 (55)	136	66 (49)	.335
CPR first responder		61 (25)		27 (26)		34 (25)	.865
Emergency medical service		56 (23)		20 (19)		36 (27)	.189
AED, n (%)							
Yes	240	94 (39)	104	53 (51)	136	41 (30)	.001
Monitored arrest, n (%)							
Yes	242	21 (9)	105	11 (11)	137	10 (7)	.384
Initial cardiac rhythm, n (%)							
Shockable	237	145 (61)	102	88 (86)	135	57 (42)	<.001
Nonshockable		92 (39)		14 (14)		78 (58)	<.001
Number of defibrillations		2.5 (± 3)		2.3 (±2)		2.7 (±3.5)	.326
Interval collapse – ROSC, n (%)							
No ROSC	221	35 (16)	95	0 (0)	126	35 (28)	<.001
<6 min.		74 (33)		62 (65)		12 (10)	<.001
6–10 min.		18 (8)		10 (11)		8 (6)	.261
>10 min.		94 (43)		23 (24)		71 (56)	<.001
Glasgow Coma Scale, n (%)							
Minor ≥13	196	14 (7)	69	13 (19)	127	1 (1)	<.001
Moderate 9-12		6 (3)		5 (7)		1 (1)	.012
Severe < 9		176(90)		51 (74)		125 (98)	<.001
Cardiac intervention *, n (%)							
PCI	242	73 (30)	105	55 (52)	137	18 (13)	
CABG		12 (5)		11 (10)		1 (1)	
ICD		26 (11)		26 (25)		0 (0)	
Therapeutic hypothermia		94 (39)		49(47)		45 (33)	
Length hospital stay (days)		5 (±8.2)		9 (±8.7)		2 (±6.3)	<.001

a P-value with Chi-square or T-test
* Patients could undergo more than one (sub)acute intervention.
Abbreviations: CA, Cardiac Arrest; CPR, Cardiopulmonary Resuscitation; AED, Automatic external defibrillator; ROSC, Return Of Spontaneous Circulation; PCI, Percutaneous Coronary Intervention; CABG, Coronary Artery Bypass Graft; ICD, Implantable Cardioverter Defibrillator

Factors associated with survival

Table 1 shows the characteristics of the 105 patients who survived until hospital discharge and the 137 patients who did not. Survivors were significantly younger, had significantly more often a CA in a public area, a witnessed arrest, an arrest of cardiac origin and a shockable rhythm, AED was more often used, a shorter time until ROSC, a GCS ≥13 during ambulance transport post CPR and a longer length of hospital stay. No significant associations with survival were found for gender, bystander CPR, number of shocks and witnessed monitored CA.

In the multivariate analyses, the variables location and use of AED were left out because of lack of independent association in the bivariate models. The time until ROSC was removed because of its almost linear relationship and strong correlation with the dependent variable survival. Logistic regression shows that four of the variables contribute significant to surviving OHCA: witnessed CA, cardiac cause, initial rhythm and GCS ≥13. (Table 2)

Table 2 Logistic regression on the likelihood of survival in OHCA patients

	p-value	**Odds Ratio**	**95% C.I. for Odds Ratio**	
			Lower	Upper
Age	0.068	0.975	0.950	1.002
Witnessed cardiac arrest	0.019	2.851	1.187	6.849
Cardiac cause of arrest	0.009	5.947	1.569	22.549
ICR shockable	0.017	2.887	1.205	6.917
GCS	0.000	1.498	1.202	1.867

C.I.=Confidence Interval
GCS = Glasgow Coma Scale
ICR= Initial Cardiac Rhythm

Discussion

This study shows that a survival rate until hospital discharge of 43% of EMS treated OHCA patients is feasible in an optimised chain of survival. The survival rate is higher than the average 14% as reported in Europe.[1,2] However, a study in the Netherlands of Waalewijn et. al.[3] also reported a high survival rate (36%) of EMS attended OHCA, be it that that study only included OHCA of cardiac origin whereas this study included all EMS treated patients. In approximately 70% of the cases the EMS decided to transport patients to the hospital (unpublished data), which is comparable to the 60% EMS treatment found in literature.[1]
In this study survivors were younger, had more often a witnessed CA, a cardiac origin of the arrest and a shockable rhythm compared to those who died. As expected, non-comatose patients (GCS ≥13 post CPR) and patients with sustained ROSC in the ambulance or ED had better chances of survival.[4]
To find an explanation for the high survival rate, a comparison with the patient characteristics and treatment in the literature should be made. The mean age (64.8 year) of the patients in the present study was in the same range as those seen in previous studies (64-67 years) [3,5,6]. In our study a relatively high proportion (67%) of the OHCA was witnessed and this was positively correlated with survival. We postulate that witnessing an OHCA contributes more to survival than CPR itself, since witnessed arrests give a higher chance of early alarm and use of an AED within minutes after collapse.

Cardiac cause of CA with an initial shockable rhythm may also partly explained the favourable outcome of this study. A systematic review reported that patients with VF or VT had a survival chance of 1 in every 4 to 7 patients compared to only 1 in every 21 to 500 patients in whom the first rhythm was asystolic.[4] In the current study, a high percentage (49%) of patients showed an initial cardiac rhythm of VF, whereas other studies reported that only 30% of the patients had an initial rhythm of VF.[8] Since VF is recorded only in the acute stage after CA, a high percentage of VF might indicate short arrival times of the ambulance service.

The use of an on site AED doubles survival, probably caused by the reduction in time to first shock.[8] Berdowski found that an AED was

used in 21% of the cases.[9] In the current study AED was used in 39% of the cases. It is plausible that in the Leiden region, which is similar to the Amsterdam area, the availability of AEDs has grown in the last 5 to 10 years, contributing to higher survival rates.

In this study 86% of the patients that reached the CCU or ICU received on average 1.4 (sub)acute interventions per person. A comparison with literature was not possible, since no studies on incidence of interventions in a comparable group were found.
EMS treated patients after OHCA discharged to their homes need cardiac rehabilitation. A recent Dutch study concluded that only a minority of the patients eligible for cardiac rehabilitation received cardiac rehabilitation.[10] With increasing survival rates probably more effort should be put in aligning the process of cardiac rehabilitation for OHCA survivors.

Conclusions

This study showed a survival rate of 43% after OHCA in a urban region in The Netherlands where an optimised chain of acute and sub-acute treatment.

Witnessed CA, cardiac origin of the arrest, shockable initial rhythm and GCS >13 post CPR were independently related to survival to hospital discharge. Availability of AED, short arrival times of EMS and (sub)acute treatment also may contribute to the success rate, but more research into the extent of the effect on survival is needed.

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Chapter 3

Cognitive problems in patients in a cardiac rehabilitation program after an out-of-hospital cardiac Arrest

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Abstract

Objective
Estimate prevalence of cognitive problems due to hypoxic brain injury in out-of-hospital cardiac arrest (OHCA) survivors referred for cardiac rehabilitation and association with quality of life as well as autonomy and participation.

Design
Prospective cohort study.

Method
Consecutive OHCA patients. The Mini-Mental State Examination (MMSE), Cognitive Failures Questionnaire (CFQ) and Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) were administered 4 weeks after the OHCA. Cognitive problems were defined if MMSE <28, CFQ >32 or IQCODE >3.6. The Impact on Participation and Autonomy Questionnaire (IPAQ) (participation/ autonomy), the SF-36 Health Survey (SF-36) (quality of life) and the Hospital Anxiety Depression Scale (HADS) (anxiety/depression) were administered. Correlations between cognitive problems and participation/autonomy and quality of life were calculated.

Results
63 of 77 patients were male (82%), median age 59 years (range 15–84). MMSE median 29 (interquartile range 28–30), CFQ mean 20.9 (SD 9.4) and IQCODE mean 3.1 (SD 0.2). Eighteen patients (23%) scored positive for cognitive problems. Significant correlations were found between MMSE and IPAQ: autonomy inside ($r=-0.38$), family role ($r=-0.26$), autonomy outside ($r=-0.32$), social relations ($r=-0.38$) and social functioning ($r=0.32$). MMSE was related to SF-36: social functioning ($r=0.32$). The CFQ was related to IPAQ: autonomy outdoors ($r=0.29$) and SF-36: bodily pain ($r=-0.37$), vitality ($r=-0.25$), mental health ($r=-0.35$) and role emotional ($r=-0.40$). The IQCODE was related to IPAQ: autonomy indoors ($r=0.26$) and to SF-36: vitality ($r=-0.33$) and social functioning ($r=-0.41$).

Conclusion
Twenty-three percent of the patients referred for cardiac rehabilitation showed cognitive problems. Associations were found between cognitive problems and several aspects of participation/autonomy and perceived quality of life.

Introduction

In Europe, out-of-hospital cardiac arrest (OHCA) has an incidence of 86.4 per 100,000 inhabitants with a survival rate of 9% until hospital discharge.[1] In the Netherlands, survival is ranging from 16 to 22% for OHCA with a cardiac cause to 43% of emergency department attended OHCA.[2,3,4]

OHCA survival can be complicated by hypoxic brain injury with subsequent cognitive impairments. A systematic review in 2009 by Moulaert et al. on cognitive impairments in survivors after OHCA retrieved 28 studies. The authors of this review concluded, based upon three large, methodologically sound, prospective studies, that cognitive problems occurred in 42% to 50% of the ventricular fibrillation OHCA survivors.[5] Cognition was measured with a broad range of extensive neuropsychological tests. Memory, attention and executive functions were most affected.

Cognitive problems can be distinguished between cognitive impairments measured with objective cognitive tests and cognitive complaints assessed with subjective questionnaires. These objective and subjective cognitive problems cause a negative effect on participation/autonomy and quality of life.[6,7] A study by Stub et al. in 2011 of patients with OHCA of suspected cardiac cause in Australia showed that of the 31% of survivors 4% was referred to a nursing home, 18% went to a rehabilitation centre and 76% went directly home.[8] Based on the 42–50% of cognitive problems found in literature a substantial amount of patients have to cope with cognitive problems at home. According to Dutch guidelines all survivors who return home are qualified for cardiac rehabilitation.[9] Currently in cardiac rehabilitation, no attention is paid to potential (mild) cognitive problems. This is a problem, since (mild) cognitive problems can have a high impact on a person's participation/autonomy and quality of life.[10] Besides for patients with brain injury treatment (cognitive rehabilitation) is proven effective.[11]

To screen for cognitive problems, the Cerebral Performance Category could be used.[12] Unfortunately, this test is not sensitive in detecting mild cognitive problems.[13] Extensive neuropsychological testing can trace mild cognitive problems, but take approximately 3 h and thus not suitable as screening.[14–16]

As screening, the widely used and validated Mini-Mental State Examination (MMSE) is often used as gold standard to detect cognitive

impairment.[17] Unfortunately the MMSE is not standardised for patients after OHCA and one can question its sensitivity. In heart failure patients the MMSE showed a sensitivity/specificity of 0.70/0.66.[18,19] It seems necessary to complement the MMSE to increase the sensitiveness. In order to list cognitive complaints, a self-perceived neuropsychological functioning questionnaire was added, the Cognitive Failures Questionnaire (CFQ).[20] Considering that some patients have an impaired awareness of illness the validated Informant Questionnaire on Cognitive Decline of the Elderly (IQCODE), was used in which partners were asked to compare the patients cognition before and after the OHCA.[21]
With the results of three tests, the cognitive impairment (MMSE) and cognitive complaints (CFQ and IQCODE), patients were advised to follow a cardiac rehabilitation program or a cardiac rehabilitation supplemented with cognitive rehabilitation. All patients who showed a deviant score on one or more parts of the screening were advised to have an intake for cognitive rehabilitation. This study describes cognitive problems in patients referred for cardiac rehabilitation after OHCA using three concise tests. In addition, the association between the presence of cognitive problems and quality of life and autonomy and participation was studied.

Methods

Study design
This study had a prospective design. Data gathered for the present study were routinely recorded in clinical care, the Medical Ethical Review Board of the Leiden University Medical Center, Leiden, The Netherlands judged this study to be outside the remit of the Dutch Medical Research Involving Human Beings Act and provided a certificate of no objection.

Patients and setting
All consecutive OHCA survivors referred for cardiac rehabilitation to the Rijnlands Rehabilitation Centre in Leiden the Netherlands were eligible for this study. Based on an estimated inclusion rate of 3 patients per month and an arbitrary wish to include 75 patients, we decided to follow all patients between 1 February 2011 and 1 February 2013. The period was extended with 3 months to reach 75 patients. OHCA patients are referred to cardiac rehabilitation by their cardiologist and admitted within 2 weeks after discharge from the hospital. Institutionalised

patients were excluded from this research.
Socio-demographic characteristics and data on the cardiac arrest were retrieved from the medical record of the rehabilitation centre.
Questionnaires on cognitive functioning, quality of life and participation/autonomy were administered to the patients and their partners within 4 weeks after the cardiac arrest by a specialised nurse at the beginning of the cardiac rehabilitation.

Assessments
Patient and OHCA characteristics included gender, date of cardiac arrest, age at time of cardiac arrest and recorded cause of cardiac arrest: myocardial infarction, cardiac arrhythmia, cardiac myopathy, myocarditis and other (i.e. heart failure, electrocution, drowning). Eligible patients were seen by specialised nurses, who helped filling in questionnaires if needed. The whole assessment for patients took approximately 55 min; for partners 10–15 min.

Cognitive functioning
Cognition was evaluated using the MMSE, CFQ and IQCODE. The MMSE is an 11-item cognitive scale ranging from 0 to 30 points and takes 10 min to conduct. The test assesses multiple domains of cognitive functioning. A cut-off score of <28 was used to determine cognitive impairments.
The CFQ is a 25-item questionnaire for self-perceived cognitive functioning and takes 10 min to complete. The CFQ provides ratings of the perception on the frequency of various cognitive slips in daily life. Items are related to memory and attention. Ponds added four questions to identify an increase of possible cognitive mistakes and how these mistakes are troublesome, aggravating or worrying someone.[22] The scale ranges from 0 to 100 and a higher score indicates worse cognitive functioning. To assess problems in self-perceived cognitive functioning we used a score of >32 as cut-off.
The partner was asked to complete the Dutch version of the short IQCODE. This version consists of 16 items, aiming at cognitive functions like everyday memory and instrumental activities of daily living and takes 10–15 min to administer.[23] The questionnaire compares the present functioning with some point in the past (situation prior to the cardiac arrest). The questionnaire has been validated for the Dutch population.[24,25] There are five response alternatives from 1, much better to 5, much worse. Higher scores indicate a greater decline: we

used the cut-off point of >3.6.[26] Cognitive problems were defined as MMSE <28, CFQ >32 or IQCODE >3.6.
To get a first impression on the relevance of the cognitive tests used, relations to participation/autonomy and perceived quality of life in daily living were studied, using the Impact on Participation and Autonomy Questionnaire (IPAQ) and the Short Form-36 Health Survey (SF-36).[27,28,29] Since depression and anxiety are confounders for cognitive complaints and quality of life, the self-report screening Hospital Anxiety Depression Scale (HADS) was obtained.[30]

Participation and autonomy
To assess social participation and autonomy, the Dutch 'Impact on Participation and Autonomy Questionnaire' (IPAQ) was used. The IPAQ focuses on autonomy and participation of people with chronic conditions. It is developed to assess disease severity, needs and outcome. Per subcategory scores range from 0 to 4. A score of 0 is normal and higher scores indicate greater hindrance in participation and autonomy or an increased problem experience. The IPAQ takes approximately 20 min to administer.

Health related quality of life
To measure the generic health status, the Dutch version of the SF-36 Health Survey was used. The SF-36 is composed of 36 questions and organised into eight scales: physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and general mental health (MH). All raw scale scores are linearly converted to a 0–100 scale, with higher scores indicating higher levels of functioning or well-being. The SF-36 takes 10 min to administer.

Anxiety and depression
Anxiety and depression were measured with the 14-item Hospital Anxiety Depression Scale (HADS) and takes <5 min to administer. The HADS consists of two 7-item scales, one for anxiety and one for depression. All items are rated on a 4-point scale (0–3). Patients with scores <8 on the 7-item scale are unlikely to have an anxiety disorder or a depression.[31] Our data shows a gap as result of changing the assessment of the cardiac rehabilitation decision support system. The HADS was suddenly left out. Due to this problem 26 patients were missed.

Analysis
Statistical analysis was performed using SPSS 22 software package. Descriptive statistics were used to present the demographic, medical and resuscitation characteristics. Mean (standard deviation) or median (range) scores and percentages of patients with cognitive problems according to fixed cut-off points of the instruments used were calculated. For the HADS the percentages of patients with possible anxiety or depressive problems were calculated using fixed cut-off points. Besides group differences were calculated on the severity of the scores of patients with cognitive problems vs. without cognitive problems using the Mann–Whitney U test.
For group differences of patients with and without cognitive problems in participation/autonomy and quality of life, as measured by IPAQ and SF-36, the Mann–Whitney U test was used. Spearman's Rho was calculated to study the relationships between baseline MMSE, CFQ and IQCODE scores and participation/autonomy (IPAQ) and quality of life (SF-36). p-Value <0.05 was used as statistically significant.

Results

Patients
Between February 2011 and May 2013, 77 patients fulfilled the inclusion criteria.
Table 1 shows the baseline socio-demographic characteristics of the patients. The majority (82%) were men, mean age 57.2 years (SD 13.8). Two-thirds of the participants (68%) lived together or were married. Of the patients 84% followed at least secondary level of education. The main cause of the OHCA was a myocardial infarction (81%). All the questionnaires filled in by patients and spouse were used in our study. Only one patient completed the questionnaires but decided afterwards to follow his cardiac rehabilitation elsewhere.

Table 1 Socio-demographic characteristics of OHCA survivors (n=77) admitted for cardiac rehabilitation

	n (%) or Mean (SD)
Age at time of cardiac arrest (range 15-84)	57.2 (13.8)
Gender	
Male	63 (82%)
Marital status*	
living together /married	52 (68%)
Education*	
primary school	6 (9%)
secondary school	33 (49%)
higher professional education	24 (35%)
Other	5 (7%)
Cause cardiac arrest	
myocardial infarction	62 (81%)
cardiac arrhythmia	5 (6%)
other	10 (13%)

SD - standard deviation
* n=68

Table 2 shows the cognitive functioning, anxiety, depression, participation/autonomy and quality of life of the participants. The median MMSE score was 29 (range 20–30) The mean score on the CFQ was 20.9 (SD 49) and on the IQCODE 3.1 (SD 0.2).

Table 2 Cognitive functioning, emotional problems, participation and quality of life of the participants

Domain	n	Cut-off	n (%) or mean (SD) or median (IQR)[#]
Age at time of CA	77		57.2 (13.8)
Gender	77		
Male			63 (82%)
Cognitive impairments			
MMSE	71	<28	29 (28-30)[#]
Cognitive functioning (self-perceived)			
CFQ	77	>32	20 (15-26)[#]
Cognitive functioning (informant)			
IQCODE	68	>3.6	3.0 (3.0-3.2)[#]
Emotional problems			
HADS Total	51	≥16	8.0 (5.7)
Depression	51	≥ 8	2 (1-4)[#]
Fear	51	≥ 8	5.1 (3.4)
Participation and Autonomy			
IPAQ			
autonomy indoors	76	---	0.8 (0.6)
family role	77	---	1.3 (0.8)
autonomy outdoors	77	---	1.3 (0.7)
social life/ relationships	77	---	1.0 (0.4)
work and education	51	---	1.6 (0.9)
Quality of Life			
Short Form-36			
physical functioning	77	---	70.7 (23.1)
role physical	77	---	30.7 (31.5)
bodily pain	77	---	69.2 (25.0)
general health	77	---	62.3 (18.1)
vitality	77	---	63.6 (20.4)
social functioning	76	---	70.4 (25.3)
role emotional	77	---	81.4 (33.5)
mental health	77	---	77.5 (17.2)

SD standard deviation; IQR Inter Quartile Range

CA Cardiac Arrest; MMSE Mini-Mental: State Examination; CFQ Cognitive Failures Questionnaire; IQCODE Informant Questionnaire on Cognitive Decline in the Elderly; HADS Hospital Anxiety and Depression Score; IPAQ Impact on Participation and Autonomy Questionnaire

Table 3 shows the scores below the cut-offs: 18 patients (25%) on the MMSE, 10 patients (13%) on the CFQ and 4 patients (6%) on the IQCODE. In total 18 patients (23%) showed cognitive problems with relatively little overlap between instruments (Fig 1.) Patients with cognitive problems did not significantly differ from patients without any cognitive problems in age (p=0.515), gender (p=0.057) or anxiety (p=0.063).

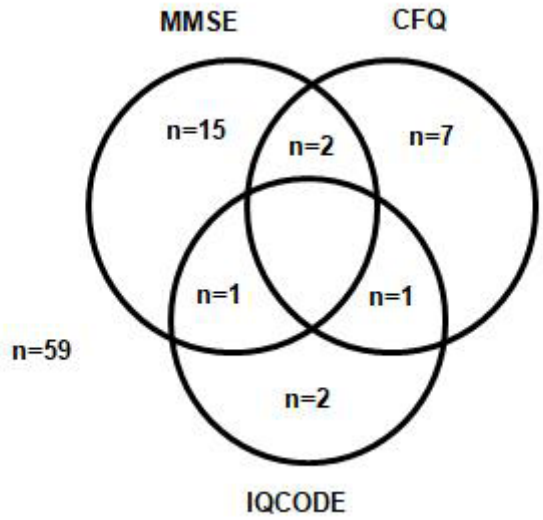

Fig. 1 Venn diagram of distribution OHCA patients who scored positive on Mini-Mental State Examination (MMSE)≥28, Cognitive Failures Questionnaire (CFQ) ≤32 or Informant Questionnaire on Cognitive decline in the Elderly (IQCODE) ≤3.6

Between patients with and without cognitive problems no significant differences were found in percentage of patients scoring positive for: fear 31% resp. 26% (p = 0.734) or depression 15% resp. 8% (p = 0.591). However on the severity of the domain depression of the HADS a significant difference was found between the patients with cognitive problems vs. the patients without cognitive problems (p = 0.025). Patients with cognitive complaints (Table 3) score worse on practically all domains of both IPAQ and SF-36.

Table 3 Group differences cognitive problems vs. no cognitive problems: Cognitive functioning, emotional problems, participation and quality of life of the participants

Domain		All patient		Cognitive problems		No cognitive problems	p-value*
	n	n (%) or mean (SD)	n	n (%) or mean (SD)	n	n (%) or mean (SD)	
Age at time of CA	77	57.2 (13.8)	18	59.6 (9.8)	59	56.5 (14.8)	.515
Gender	77		18		59		
Male		63 (82%)		12 (67%)		51 (86%)	.057
Cognitive functioning							
MMSE	71	28.8 (1.6)	18	27.3 (2.6)	53	29.2 (0.7)	.002
CFQ	77	20.9 (9.4)	20	29.1(11.2)	57	18.4 (7.2)	.001
IQCODE	68	3.1 (0.2)	16	3.3 (0.4)	52	3.1 (0.1)	.119
Emotional problems							
HADS Total	51	8.0 (5.7)	13	10.9 (4.2)	38	7.1 (5.9)	.018
Depression	51		13	4.5 (3.2)	38	2.4 (2.8)	.025
Fear	51		13	6.4 (1.9)	38	4.7 (3.7)	.063
Participation and Autonomy							
IPAQ							
autonomy indoors	76	0.8 (0.6)	17	1.2 (0.8)	59	0.8 (0.5)	.022
family role	77	1.3 (0.8)	18	1.8 (1.2)	59	1.1 (0.6)	.010
autonomy outdoors	77	1.3 (0.7)	18	1.7 (0.9)	59	1.1 (0.6)	.004
social life/ relationships	77	1.0 (0.4)	18	1.1 (0.5)	59	0.9 (0.4)	.145
work and education	51	1.6 (0.9)	10	1.8 (1.0)	41	1.6 (0.8)	.320
Quality of Life							
Short Form-36							
physical functioning	77	70.7 (23.1)	20	58.4 (27.5)	57	74.4 (20.4)	.034
role physical	77	30.7 (31.5)	20	15.3 (15.2)	57	35.5 (33.7)	.035
bodily pain	77	69.2 (25.0)	20	59.4 (25.1)	57	72.2 (24.4)	.064
general health	77	62.3 (18.1)	20	56.8 (15.2)	57	64.0 (18.6)	.225
vitality	77	63.6 (20.4)	20	54.4 (23.5)	57	66.4 (18.7)	.037
social functioning	76	70.4 (25.3)	19	54.4 (25.4)	57	75.0 (23.6)	.003
role emotional	77	81.4 (33.5)	20	66.7 (39.6)	57	85.9 (30.5)	.004
mental health	77	77.5 (17.2)	20	68.2 (15.6)	57	80.3 (16.7)	.018

CA Cardiac Arrest; MMSE Mini-Mental: State Examination; CFQ Cognitive Failures Questionnaire; IQCODE Informant Questionnaire on Cognitive Decline in the Elderly; HADS: Hospital Anxiety and Depression Score; IPAQ: Impact on Participation and Autonomy Questionnaire

Table 4 shows that the MMSE relates to the IPAQ categories autonomy inside (r = −0.375), family role (r = −0.256), autonomy outside (r = −0.318) and social relations (r = −0.381). The CFQ related best to the IPAQ autonomy outside (r = 0.287). The IQCODE showed a relation with the IPAQ autonomy inside (r = 0.260).
The significant relation between the MMSE and the SF-36 was visible in social functioning (r = 0.317). The CFQ showed a significant relation with the SF-36 in bodily pain (r = −0.366), vitality (r = −0.250), mental health (r = −0.351) and role emotional (r = −0.400). The IQCODE was significantly related to the SF-36 in vitality (r = −0.332) and social functioning (r = −0.412). The HADS subscales depression and fear show no significant relation with MMSE (resp. r = 0.52 and 0.82), CFQ (resp. r = 0.15 and 0.06) or IQCODE (resp. r = 0.36 and 0.62).

Table 4 Spearman Correlations of total group (N=77) on cognitive functioning vs. participation, quality of life and depression.

	MMSE		**CFQ**		**IQCODE**	
	r_s	p-value	r_s	p-value	r_s	p-value
IPAQ						
autonomy indoors	-.38	.001	.20	.091	.26	.032
role family	-.26	.031	.16	.153	.12	.330
autonomy outdoors	-.32	.007	.29	.011	.14	.271
social relations	-.38	.001	.16	.176	.10	.433
work and education	-.20	.168	.17	.228	.25	.093
SF-36						
physical	.17	.161	-.16	.176	-.24	.051
bodily pain	.03	.818	-.37	.001	-.13	.277
role physical	.20	.091	-.05	.650	-.10	.443
general health	.15	.214	-.12	.313	-.07	.578
vitality	.13	.266	-.25	.028	-.33	.006
social functioning	.32	.007	-.17	.139	-.41	.001
mental health	.15	.200	-.35	.002	-.19	.115
role emotional	-.10	.414	-.40	.000	-.11	.377
HADS						
depression	.10	.522	.21	.147	.14	.364
fear	-.03	.819	.27	.055	.08	.620

MMSE Mini-Mental State Examination; CFQ Cognitive failures questionnaire; IQCODE Informant Questionnaire on Cognitive Decline in the Elderly; IPAQ Impact Profile on Autonomy Questionnaire

Discussion

This study shows that cognitive problems occur in 23% of patients referred for cardiac rehabilitation. A correlation between cognition and participation/autonomy and quality of life was found in the categories autonomy in- and outside, family role, social relations/ social functioning, bodily pain, vitality, mental health and emotional.
The 23% cognitive problems in OHCA survivors found in this study is lower than found in literature (42–50%). Maybe not all patients are actually referred for rehabilitation or the sensitivity of the tests used is insufficient. In the Leiden region, 80% of the OHCA survivors living in the affiliated area of the rehabilitation centre are referred for cardiac rehabilitation. The 20% non-referrals went to nursing homes or had comorbidity preventing participation in rehabilitation (unpublished data). These patients might have higher chances of cognitive impairments.
The mean MMSE score found in this study 28.8 (SD 1.6) is similar as found in a study of Mateen in survivors 6 months after the cardiac arrest due to ventricular fibrillation (28.6). Besides the objective MMSE, commonly used as gold standard, the subjective CFQ and the IQCODE were used to assess cognitive functioning. The CFQ retrieved 7 patients with cognitive complaints that were not found with the MMSE and the IQCODE identified an additional 2 patients.

In this study, the CFQ retrieves more and for 70% other patients than the MMSE. It is important though to take the influence of concernedness or depression into account since these factors may lead to higher scores on the CFQ, therefore the HADS was administered. Between patients with and without cognitive problems no significant differences were found in percentage of patients scoring positive for: fear 31% resp. 26% ($p = 0.734$) or depression 15% resp. 8% ($p = 0.591$). However on the severity of the domain depression of the HADS a significant difference was found between the patients with cognitive problems vs. the patients without cognitive problems ($p = 0.025$).

The contribution of the IQCODE seems limited. This might be caused by the early moment that informants are questioned. Patients only recently had an OHCA and are only just dismissed from hospital at time of the screening. Cognitive impairments might not yet be visible to the

partner. Besides, one could hypothesise that euphoria, that patient is still alive, might influence outcomes. Further research on the use of the IQCODE is therefore necessary.

In this study, the association of the used cognitive test and questionnaires and the experienced participation/autonomy and quality of life was obtained. Correlations were only moderate to weak. This can be explained by the fact that participation/autonomy and quality of life are likely to be influenced by limitations in cognitive functioning, there are many other potential factors which may have an impact. Patients who scored below the MMSE cut-off point experienced more participation/autonomy problems (IPAQ) on all domains except on work. This seems plausible since patients are not working at the moment of the questionnaire. For patients that scored low on the MMSE (<28), social functioning was mainly affected with regard to quality of life (SF-36).

The subjective CFQ and IQCODE show a relation with participation/ autonomy on respectively autonomy outdoors and indoors and correlate with multiple dimensions of quality of life. Although correlations with the different domains are weak to moderate it does indicate possible coping problems. By taking objective cognitive impairments and subjective cognitive complaints into account a combination of the MMSE, CFQ and IQCODE seems a first step towards a short (approximately 20 min) cognitive screening after an OHCA.
For patients showing cognitive problems on any of these tests, the administration of more extensive neuropsychological tests is warranted in order to provide a tailored cognitive rehabilitation program. Moulaert at al. also found that an early intervention program which pays attention towards cognitive problems after OHCA is very welcome by patients and spouse.

We chose to administer the questionnaires 4 weeks after the OHCA since this is the start point of the rehabilitation program. Probably, this moment does not reflect the end-point situation and cognitive improvement might occur during the rehabilitation period.

Our data being gathered as part of a cardiac rehabilitation program also causes another drawback of this study because only a limited amount of medical data and data concerning the OHCA in this specific

population is available. More extensive data on the characteristics of the OHCA of this population are described in previous research of Boyce, that described survival of OHCA patients transferred to emergency unit in the region Leiden. (73% male, median age 65 years, 76% of cardiac origin and 5% shockable rhythm, 74% witnessed, 76% bystander cardiopulmonary resuscitation and 39% automatic external defibrillator.)

Another limitation is the cognitive and behavioural status of patients prior to the OHCA. Although partners are asked to fill in the IQCODE and compare it with the situation prior to the OHCA this is a subjective point of view. Due to the unexpected nature of OHCA most of the time no objective data before the CA is available. Another drawback is the lack of a gold standard as screening to identify (mild) cognitive problems. Based on poor outcomes on one of the three cognitive measures, participants are assigned to either one of the two groups: with or without cognitive problems. The evidence for making such group distinction will remain open but is a first step forward towards a screening for cognitive problems of patients after OHCA. In future a decent comparison should be made between the screening and extensive neuropsychological tests serving as the gold standard for patients after OHCA.

Conclusion

This study describes the use of a simple cognitive assessment in patients referred for cardiac rehabilitation after OHCA. Using the MMSE 10% has cognitive impairments, using the CFQ 13% has cognitive complaints. Using the combination of MMSE, CFQ and IQCODE 23% of cardiac rehabilitation referred patients after OHCA experience cognitive problems. The MMSE and the CFQ seem to be rather complementary. This study shows that patients with cognitive problems due to OHCA experience lower levels of participation/autonomy and decreased quality of life (SF-36).

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Chapter 4

Out-of-hospital cardiac arrest survivors with cognitive impairments have lower exercise capacity

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Abstract

Background
Hypoxic brain injury is described in up to 40% of survivors after out-of-hospital cardiac arrest (OHCA). Besides cognitive impairments, lack of circulation may also affect exercise capacity. It is not known if exercise capacity of patients with cognitive impairments differs from other OHCA survivors.

Methods
This retrospective cohort study included patients ≥18 years with myocardial infarction (MI) as cause of OHCA admitted for cardiac rehabilitation between February 2011 and April 2014. Data in socio-demographic, OHCA and medical interventions were retrieved. Cognitive functioning was determined with the Mini-Mental State Examination, Cognitive Failures Questionnaire and the Informant Questionnaire on Cognitive Decline in the Elderly. Exercise capacity (VO2peak), workload (Watts) and blood pressure (mmHg) were measured at maximum cardiopulmonary exercise. Heart rate (bpm) was measured at rest and maximum exercise and Metabolic Equivalents of Tasks (MET) were calculated.

Results
65 patients after OHCA caused by MI were included (85% male, median age 60 years). Of 53 patients Cardio Pulmonary Exercise Test data was available of which nine patients showed cognitive impairments.
Significant differences ($p < 0.05$) in exercise capacity were found between patients with and without cognitive impairments: VO2peak (median 14.5 vs 19.7 ml/kg/min), workload (median 130.0 vs 143.5 W) and MET's (median 4.1 vs 5.6).

Conclusion
Based on this small study, there seems to be a correlation between cognitive impairments and lower exercise capacity in patients referred for rehabilitation after OHCA caused by MI. It seems sensible for rehabilitation programs to take the lower exercise capacity of patients with cognitive impairments into account.

Introduction

In Europe survival rate after out-of-hospital cardiac arrest (OHCA) is on average 10% [1]. Initial shockable rhythm show higher survival rates (44%) when compared to non-shockable rhythm (3%) [2]. Recent studies show higher survival rates in the Netherlands [3,4]. These higher survival rates might be due to short arrival times ambulance and increased use of Automatic External Defibrillators by bystanders.
OHCA can cause hypoxic brain injury which may lead to cognitive impairments [5]. In a systematic review, Moulaert et al. reported cognitive impairments in 42%-50% of all OHCA survivors [6]. One could postulate that patients with a more severe cardiac event have higher chances of cerebral oxygenation problems leading to cognitive impairments. Besides, the lack of circulation may not only cause cognitive impairments, but may also affect the cardiac muscle and thus affect exercise capacity [7]. However, data on this particular topic is scarce.
Up to 50% of the patients that survive an OHCA have a Myocardial Infarction (MI), and thus underlying cardiovascular disease, as cause of their cardiac arrest [8]. Exercising after MI significantly increases VO2peak (peak oxygen uptake), metabolic equivalents of tasks (METs) and anaerobic threshold (AT) [9–12]. Besides we know that physical exercises have a positive effect on both cognitive impairments and many of the established risk factors for cardiovascular disease [1,13,14]. Literature shows a relation between cardiovascular risk factors (CVR) and cognitive impairments: vascular disease and midlife hypertension, are correlated to progressive loss of memory and cognitive functions. Vascular cognitive impairments (VCI) is the umbrella term that covers the spectrum from mild cognitive deficits to vascular dementia [15–17]. Since many of the OHCA survivors suffer from cardiovascular disease, this may implicate that part of the cognitive impairments in the OHCA survivors were already present before the OHCA [18].
The aim of this prospective study is to determine whether there are differences in exercise capacity between MI-induced OHCA survivors with and without cognitive impairments. The results of this study are relevant for the design of rehabilitation programs after OHCA.

Methods

Study design

Data in this retrospective cohort study were collected as part of the integrated care pathway for OHCA survivors of the Rijnlands Rehabilitation Centre (RRC) in Leiden, the Netherlands. As all data were gathered for routine clinical care, the Medical Ethical Review Board of the Leiden University Medical Centre (LUMC) judged this study to be outside the remit of the Dutch Medical Research Involving Human Beings Act and provided a certificate of no objection.

Participants

All data of the consecutive OHCA survivors referred for integrated cardiac rehabilitation between 1 February 2011 and 30 April 2014 to the Rijnlands Rehabilitation Centre were included. Patients were selected if age ≥18 years and OHCA was caused by MI. Probable MI, possible MI and in-stent thrombosis with deficits on perfusion scan or Magnetic Resonance Imaging (MRI) were considered as MI. Patients were excluded if: MI occurred >48 h before OHCA; the cardiac arrest occurred in hospital.

In order to create comparable groups, this study only pertained patients with a MI as cause of the cardiac arrest. Their CVR factors are also taken into account. Integrated rehabilitation care pathway for OHCA survivors To achieve patient-centred cardiac and cognitive rehabilitation to all OHCA survivors and their spouses, cardiac and cognitive rehabilitation is coordinated in an integrated care pathway [19].

The integrated rehabilitation pathway, as used in the Rijnlands Rehabilitation Centre, focuses mainly on secondary prevention: restoration of exercise capacity and optimal cognitive functioning in order to achieve optimal participation in society, with minimal burden for spouses and society. Besides, tertiary prevention takes place in order to diminish the chance of new cardiovascular events. Therefore education was provided to all CA survivors and their family and a simple screening for cognitive problems was performed containing the Mini-Mental State Examination (MMSE), Cognitive Failure Questionnaire (CFQ) and the Informant Questionnaire on Cognitive Decline of the Elderly (IQCODE). Patients with possible cognitive impairments followed cardiac rehabilitation in a smaller group that was supervised both by a cardiac and a cognitive oriented physical therapist. Besides, patients

with cognitive impairments were offered an appointment with the cognitive rehabilitation physician. If needed, cognitive rehabilitation was started directly after the cardiac rehabilitation program [21].

Assessments

OHCA survivors were registered prospectively in the database of the integrated care path for OHCA survivors of the RRC. Data were imported from the Cardiac Rehabilitation Decision Support System 3.1.0 (Mediscore CARDSS, Itémedical, the Netherlands) and the medical record.

Socio-demographic characteristics, MI (location, Left Ventricle function: good >60%; reasonable 45–60%; moderate 35–45%; poor <35% based on the echo), data on acute treatment (Percutaneous Coronary Intervention, Coronary Artery Bypass Grafting and Internal Cardioverter Defibrillator) and risk factors (hypertension, hypercholesterolemia, diabetes mellitus, nicotine abuse and previous MI) were recorded. As part of the integrated care pathway all patients were screened on cognitive functioning within 2 weeks after hospital discharge and before the Cardio Pulmonary Exercise Testing (CPET). Unfortunately, no gold standard is available as a cognitive screening. The gold standard, to detect cognitive impairments, is an extensive neuropsychological test, that takes several hours. The MMSE, though no gold standard, is an often used short test to screen for cognitive deficits [20]. However, this test has a ceiling effect. In order to be more sensitive than the MMSE alone, we added the CFQ questionnaire about cognitive slips [21]. Besides we added the only well validated questionnaire for the recognition of cognitive impairments by caregivers: the IQCODE [22].

The MMSE is a well validated short, 24 item, face-to-face performed cognitive screening (scale ranging from 0 to 30 points). The test assesses multiple domains of cognitive functioning: orientation, memory, concentration, language and praxis. Unfortunately, the MMSE has a ceiling effect, which negatively influences the sensitivity. In this study therefore a relatively high cut off score of <28 was used based on the results of Bour et al. [23].

The CFQ is a 25 item questionnaire in which patients rate their perception of frequency of various cognitive slips in daily life. The items are related to memory and attention. The questionnaire takes about 10 min to complete and the scale ranges from 0 to 100. A higher score indicates worse perceived cognitive functioning. A score of >32 was used as cut off, based on the mean score of 31.8 (SD 11.1) Ponds

found in healthy subjects [24].
The partner was asked to complete the Dutch version of the short IQCODE. The 16 item questionnaire aims at cognitive functions like everyday memory and instrumental activities of daily living and compares the present functioning with the situation prior to the cardiac arrest. A higher score (range from 1 to 5) indicates a greater decline. Based on the findings of Jorm et al. we used the cut-off point of >3.6 [24].
Cognitive impairments were considered present if the score on the MMSE was <28 or the IQCODE was >3.6 or the CFQ was >32. Exercise capacity was measured 6–8 weeks after the MI, at the start of the cardiac rehabilitation by means of CPET on a bicycle ergometer with the following parameters: VO2peak; heart rate, blood pressure (systolic and diastolic), MET's and anaerobic threshold.
A twelve lead ECG was made during the CPET to retain heart rate. During CPET blood pressure was measured with a blood pressure monitor which was automatically controlled by the computer by using a cuff on the right arm of the patient (Riva-Rocci method) [25]. Blood pressure at maximum exercise and heart rate at rest and at maximum exercise were used for analysis.
Increasing the intensity of exercise will cause the heart rate and the systolic blood pressure to increase [26]. Systolic blood pressure and heart rate at maximum exercise were collected in order to be informed about the maximum effort patients gave.

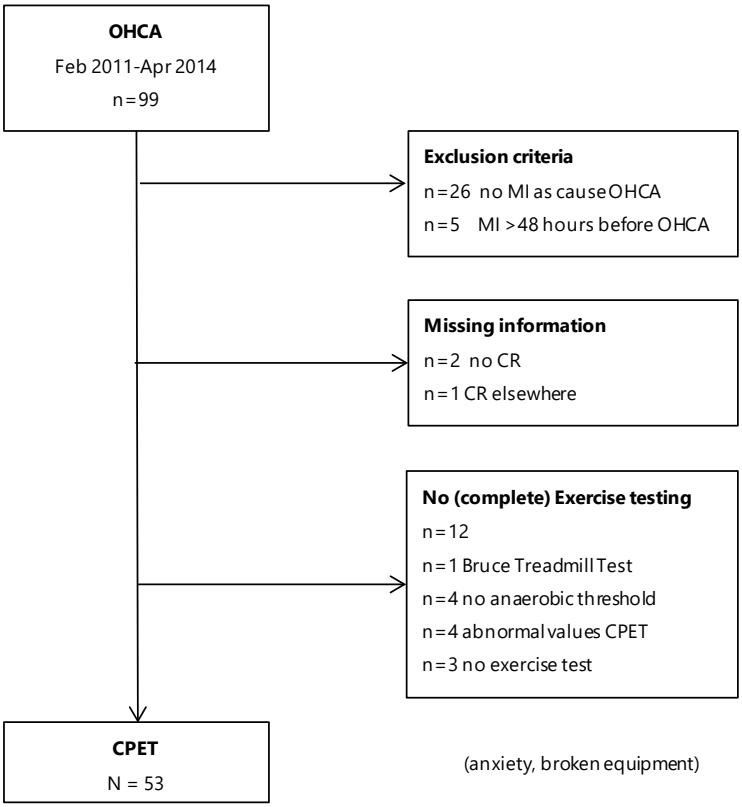
Statistical analysis
All statistical analyses were performed using IBM SPSS Statistics 22 software package. Descriptive statistics were used to present socio-demographic characteristics, OHCA and treatment results of CPET. Differences in exercise capacity between patients with and without cognitive impairments were determined with the Mann-Whitney U test. Because of the small sample sizes, dichotomous variables were tested 2-sided with use of the Fisher's exact test, unknown variables were left out. For all analyses a p-value of ≤0.05 was used as statistically significant.

Results

Participants

Between 1 February 2011 and 30 April 2014, 99 OHCA survivors were referred for cardiac rehabilitation. Patients were excluded when the OHCA was not caused by an MI (n = 26) or in case of not starting cardiac rehabilitation (n = 3). In total 65 patients with myocardial infarction were included for this study (Fig. 1) of which 53 patients had an adequate CPET.

Figure 1. Flow chart of patient inclusion



OHCA Out of Hospital Cardiac Arrest; MI Myocardial Infarction; CR Cardiac Rehabilitation; CPET Cardio Pulmonary Exercise Test

In 12 of the 65 patients no adequate CPET data were available. One patient was excluded because the Bruce Treadmill Test was performed instead of CPET. In four patients no AT was found caused by extreme tiredness before reaching AT. In five patients no CPET data was available due to a temporarily technical defect in the recording of the data. One patient was too afraid to start CPET and of one patient no CPET data could be retrieved in medical record other than CPET that was performed. Three of these 12 patients had cognitive impairments based on the MMSE, CFQ or IQCODE.

Characteristics of patients admitted for rehabilitation

Table 1 shows the sociodemographic and disease characteristics of the patients. The time between OHCA and CPET (median 4, range 2–32 weeks) was within the aimed time frame of maximal 8 weeks after the OHCA as protocolled in the rehabilitation centre. Although it was not a significant difference ($p = 0.192$) it seems that patients with cognitive impairments start later with cardiac rehabilitation (10 weeks vs 4 weeks) than patients without cognitive impairments.

Nine of the remaining 53 patients had cognitive impairments after OHCA according to one or more of the three instruments for cognitive functioning: 4 scored below the cut-off on the MMSE, 3 on the IQCODE and 3 on the CFQ (one patient scored on both CFQ and IQCODE).

Table 1 shows that, apart from relatively fewer patients with diabetes in the group of patients without cognitive impairments ($p = 0.03$), there were no statistically significant differences between the two subgroups. Left ventricular function was more often unknown for patients with cognitive deficits (56% vs 25%).

Table1 Characteristics at baseline of 65 OHCA survivors with myocardial infarction

	all patients	CPET			
		total patients	no cognitive impairments	cognitive impairments	p-value[a]
	n=65	n=53	n=44	n=9	
Age in years, median (range)	60 (36-84)	61 (10.1)	60 (42-84)	62 (49-74)	.492
Body Mass Index, median (range)	26.1 (19.5-37.9)	26.4 (19.5-37.9)	26.2 (19.5-33.3)	26.8 (21.5-37.9)	.421
Time CPET after CA (week), median (range)	4.4 (2.0-31.7)	4.4 (2.4-31.7)	4.3 (2.4-31.7)	9.9 (2.4-18.7)	.192
Male gender, n (%)	55 (84.6)	45 (84.9)	38 (86.4)	7 (77.8)	.611
Infarct location, n (%)					1.000
Anterior, anterolateral or anteroseptal	25 (38.5)	18 (33.9)	15 (34.1)	3 (33.3)	
Inferior, infero-posterior or apical	23 (35.4)	20 (37.7)	17 (38.6)	3 (33.3)	
NSTEMI	3 (4.6)	2 (3.8)	2 (4.5)	-	
Location unknown	14 (21.5)	13 (24.5)	10 (22.7)	3 (33.3)	
Acute treatment, n (%)					
PCI	54 (83.1)	42 (79.2)	35 (79.5)	7 (77.8)	1.000[a]
CABG	10 (15.4)	10 (18.9)	8 (18.2)	2 (22.2)	1.000[a]
ICD	8 (12.3)	8 (15.1)	5 (11.4)	3 (33.3)	.124[a]
Beta blockers, n (%)	64 (98)	51 (96.2)	43 (97.7)	8 (88.9)	.313
Risk factors, n (%)					
Diabetes	5 (7.7)	5 (9.4)	2 (4.5)	3 (33.3)	.030
Hypertension	29 (45.3)	24 (45.3)	20 (45.5)	4 (44.4)	1.000
Hypercholesterolaemia	27 (42.2)	22 (41.5)	17 (37.8)	5 (55.6)	.464
Nicotine use before CA	29(44.6)	25 (47.2)	20 (44.7)	5 (55.6)	.719
Left ventricle function, n (%)					.381
good	23 (35.4)	21 (39.6)	18 (40.9)	3 (33.3)	
reasonable	7 (10.8)	6 (11.3)	6 (13.6)	-	
moderate	10 (15.4)	7 (13.2)	7 (6.8)	-	
poor	3 (4.6)	3 (5.7)	2 (34.1)	1 (11.1)	
unknown	22 (33.8)	16 (30.2)	11 (4.5)	5 (55.6)	
Previous myocardial infarction	6 (9.2)	5 (9.4)	3 (6.8)	2 (22.2)	.196

OHCA out of hospital cardiac arrest, CPET cardio pulmonary exercise testing, NSTEMI Non ST-segment elevation myocardial infarction, PCI Percutaneous coronary intervention, CABG Coronary artery bypass graft, ICD Implantable cardioverter defibrillator, CA cardiac arrest
[a] Fisher exact or Mann-Whitney U test

In Table 2 parameters of exercise capacity of the total CPET group and the two subgroups are presented. No differences were found for heart rate, systolic and diastolic blood pressure in rest and at maximum exertion.

Patients with cognitive impairments showed a significant lower VO2peak (median 14.5 ml/kg/min) if compared with patients with no cognitive impairments (median 19.7 ml/kg/min).

This difference was also consistently found for workload (p = 0.004) and METs (p = 0.003). Patients with cognitive impairments showed a lower workload than patients with no cognitive impairments (median 130.0; IQR 103.0–151.0 vs median 143.5; IQR 114.5–167.5) and lower METs (median 5.6; IQR 4.9–7.1 vs median 4.1;IQR 3.3–5.2 MET).

Table 2 Values Cardiopulmonary exercise testing (CPET) at baseline.

	all patients	**cognitive impairments**		
	n=53	No (n=44)	Yes (n=9)	p-value*
	median (IQR)	median (IQR)	median (IQR)	
VO2peak (ml/kg/min)	19.3 (15.2-23.9)	19.7 (16.9-24.8)	14.5 (11.3-18.1)	.004
VO2AT (ml/kg/min)	15.6 (13.1-18.4)	16.4 (14.0-19.5)	13.8 (9.7-15.5)	.006
Load (W)	139.0 (110.5-165.0)	143.5 (114.5-167.5)	130.0 (103.0-151.0)	.004
Load (%)	90.0 (73.5-111.5)	102.0 (79.5-116.0)	68.0 (52.0-86.5)	.006
Load AT (W)	98.0 (73.5-112.5)	99.0 (78.0-117.8)	72.0 (60.5-94.5)	.021
METs	5.5 (4.4-6.7)	5.6 (4.9-7.1)	4.1 (3.3-5.2)	.003
METs (%)	81.0 (62.5-96.00)	89.0 (69.3-97.8)	61.0 (54.0-70.5)	.003
HRrest (beat/min)	61.0 (52.5-70.5)	60.0 (51.3-69.5)	65.0 (61.0-74.0)	.115
HRmax (beat/min)	120.0 (107.0-135.0)	120.5 (107.3-141.8)	112.0 (104.5-125.0)	.184
RR_{max} systolic (mmHg)	185.0 (155.0-200.0)	187.0 (156.5-205.3)	177.0 (139.5-192.5)	.142
RR_{max} diastolic (mmHg)	77.0 (72.0-85.0)	78.5 (75.0-88.75)	75.0 (62.5-80.0)	.086

VO2peak Peak oxygen consumption, VO2AT Oxygen consumption anaerobic threshold, W Watt, MET Metabolic Equivalent of Tasks HRrest Heart Rate in rest, HRmax Heart Rate at maximum exercise; RRmax Riva-Rocci at maximum exercise.
* Mann-Whitney U test

Discussion

Based on this small study, there seems to be a correlation between cognitive impairments and lower exercise capacity in patients referred for rehabilitation after OHCA caused by MI. Effects were seen in VO2peak, work load and METs.

In literature a broad range of VO2peak is found in patients after MI with a variation of 13.9 up to 32.3 ml/kg/min [11,12]. Our patients after OHCA caused by MI showed a median VO2peak of 19.3 ml/kg/min, which is within range of patients after MI without OHCA. Even the cognitive impaired patients, that score significantly below patients without cognitive impairments, score within this range (14.5 ml/kg/min). Consistent data were found for workload and METs in which also significant differences were found between patients with and without cognitive impairments (respectively 130W vs 143.5W and 4.1 vs 5.6 MET). Although the aetiology of the difference in exercise capacity for OHCA patients with and without cognitive impairments is not yet clear one might postulate that patients with cognitive impairments suffered from more severe hypoxia, which may also effect other organ systems. A study by Picano et al. supports this: They describe the influence of different physiological characteristics of cardiovascular hemodynamics and their mutual cohesion. One of their conclusions is that cognitive performance is associated with the maximum aerobic exercise capacity which is dependent on size infarction and ventricular function [9]. Unfortunately one of the limitations of this study is the lack of data indicating the size of the infarction, as could have been measured for instance with an area under the curve estimations of creatine kinase. Also, left ventricular function was not conclusive due to small numbers and >50% missing data in the cognitive impaired group.

One could also argue that patients with a lower exercise capacity and cognitive impairments after OHCA suffered already premorbid from a more severe cardio vascular disease. This theory is supported by the higher observed incidence of diabetes in the cognitive impaired group, since patients with diabetes have an increased risk of both cardio vascular diseases and cognitive deficits [18,27,28].

This idea is supported by the findings of Gottesman et al. They found that cardio vascular disease, hypertension and elevated systolic blood

pressure, is associated with more cognitive decline [29]. A bias in this study might be the relatively low percentage of patients with cognitive impairments after OHCA, since in this study we only found 18.8% of the patients to have cognitive impairments which is remarkably lower than the 42–50% found in literature [7]. Most probably, this difference can be explained by a selection bias: only patients that are fit enough are actually referred for rehabilitation after hospital discharge. Due to a structured care pathway in the affiliated area of the rehabilitation centre 80% of the OHCA survivors are referred for cardiac rehabilitation [30]. The 20% non-referrals went to nursing homes or had comorbidity preventing participation in rehabilitation (unpublished data). The non-referral group might have higher chances of cognitive impairments.

Another bias in this study might be caused by the screening. The IQCODE is not used in its original version ('10 years decline' in the original version versus 'prior to the cardiac arrest'). Thereby the cut-off value as used for the original version of the IQCODE (score 3.6) is not validated for the much shorter time-frame which is used in this study. Also for the CFQ no validated cut-off point was available and we used a cut-off at 32 (instead of a cut off at 21, mean –1SD). One might argue that the cut-offs, used in order not to overlook any patients, might be too wide [24,26].

This study indicates that patients with cognitive impairments after OHCA may have more severe cardiac impairments. Cognitive impairments may have a negative effect on the outcome of cardiac rehabilitation [31,32]. On the other hand physical exercises have a positive effect on both cognitive impairments and many of the established risk factors for cardiovascular disease [33–35].

We therefore strongly suggest that all survivors of cardiac arrest have both a check-up for cognitive impairments and cardiac impairments when attending a rehabilitation program. The cognitive screening should contain at least the MMSE or Montreal Cognitive Assessment. The screening can be performed during a face-to-face contact by a specialised nurse or physician assistant before the start of the outpatient rehabilitation program. In our experience, taking cognitive impairments into consideration prevents drop out of the cardiac rehabilitation group. The cognitive screening and psycho-education are highly appreciated by all patients and spouses, taking away

worries for those without cognitive impairments and providing the opportunity to tailor the rehabilitation program to individual needs for those with impairments. For patients with severe cognitive deficits, we recommend not to forget to perform CPET in order to be informed about their cardiac capacity.

Rehabilitation programs can take the lower exercise capacity of patients with cognitive impairments into account in order to provide individualised patient-centred rehabilitation care aiming at optimal participation.

Conclusion

This study shows that patients with cognitive impairments seem to have a lower exercise capacity when starting a rehabilitation program than patients without cognitive impairments after OHCA caused by MI. More research in larger prospective studies is needed.

Conflicts of interest

The authors report no conflicts of interest.

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Chapter 5

Rehabilitation after Cardiac Arrest: Integration of Neurologic and Cardiac Rehabilitation

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Abstract

Cognitive impairments are common after resuscitation. Severe cognitive impairments are easily recognised. Mild cognitive impairments are much more difficult to spot. Given the influence of cognitive problems in daily functioning it is important to identify cognitive impairments in an early stage. Also emotional problems, mainly depression and fear, are common in this group of patients.
To optimise the care for patients after an out-of-hospital cardiac arrest the rehabilitation should focus on the physical approach through cardiac rehabilitation and on the brain injury and the associated cognitive impairments.
The goal of rehabilitation after a cardiac arrest is to provide excellent patient-centred cardiac and cognitive rehabilitation to all patients and their spouses in order to achieve optimal participation in society, with minimal burden for spouses and society.
To achieve this, cardiac and cognitive rehabilitation needs to be coordinated in an integrated care path.
Out of-hospital cardiac arrest (OHCA) is one of the main causes of death around the globe. A systematic review including 67 peer-reviewed studies published from 1990 to 2008 concludes that the global average incidence is 55 adult OHCAs of presumed cardiac cause per 100.000 person-years.[1] Based on this systematic review an average survival following adult OHCA of 7% was found. In Europe the incidence of emergency medical service- (EMS-) attended OHCA is 86.4 per 100,000 inhabitants per year. The review reports that 60% of the patients in Europe are treated by EMS after OHCA and 9% of these patients survive to hospital discharge. Overall the most common cause of CA is cardiovascular disease and coronary ischemia.[2,3]
After surviving an OHCA patients often experience physical exercise problems as result of the event. Another potential consequence of the CA is the interruption of blood circulation to the brain. This can lead to brain injury. Irreversible damage to the brain already occurs after several minutes. The brain injury can be very diffuse and therefore the neurological consequences are diverse. To decrease the severity of the brain injury patients receive targeted temperature management (TTM) in the hospital. Despite the measures in the (sub) acute phase an estimated 40%-50% of all survivors have still cognitive problems half a year after the CA.[4]
The majority of patients that survive an out-of-hospital cardiac arrest

(OHCA) are –according to European guidelines- eligible for cardiac rehabilitation.[5,6] We advocate that besides a physical approach through cardiac rehabilitation, also the brain injury and the associated cognitive problems should be taken into account through cognitive rehabilitation.

Cardiac consequences after Cardiac Arrest

Due to the cardiac cause of the OHCA, the majority of patients spend the rest of their lives as cardiac patients. After lifesaving interventions such as percutaneous coronary intervention, coronary artery bypass grafting, and TTM, patients might have to take medication, live with an implantable cardioverter defibrillator, have a decreased exercise span, or are advised to make major life changes to optimize their health and to prevent recurrence.

Emotional problems and fatigue after Cardiac Arrest

Besides physical problems, patients also experience emotional problems. Of all patients after a CA, 75% develop emotional problems. Depression is present in 14 to 45% of survivors, anxiety in 13 to 61%, and symptoms of posttraumatic stress in 19 to 27%.[7,8]

Fatigue is also often reported after CA. Even several years after a CA, 56% of the survivors suffer from severe fatigue.[9]

Emotional problems and fatigue have a significant impact and can affect a patient's daily functioning, return to work, and quality of life. The prognosis for cardiac patients who live on their own is even worse. The literature reveals that social support is an important precondition for physical and mental recovery of the heart patient.[10,11]

Cognitive impairments after Cardiac Arrest

Most of the CA survivors seem to have a good neurologic outcome. However, besides the emotional problems and fatigue, cognitive impairments are also common.[4,8,9,12] Half of the survivors report cognitive impairments.[4] Memory, attention, and executive functioning are most affected.4 The cognitive impairments can be severe, but are mostly mild. Mild cognitive problems are often not recognized in time by health care professionals. Cognitive problems cause a negative effect on participation/autonomy and quality of life.[13]

A well-known predictor of cognitive functioning after traumatic brain injury is coma duration.[14] However, for survivors of OHCA, evidence on the relation between coma duration and outcome is scarce.[15] The

question whether TTM protects against cognitive disabilities is not yet solved.[16,17] One might even argue that cognitive impairments are not necessarily caused by CA alone but by cardiovascular disease in general. Lilja et al compared outcome of CA survivors with an age- and gender-matched control group with similar cardiovascular risk factors, but with acute myocardial infarction instead of CA. Surprisingly, they found only very minor differences between groups.[18]
It is important that patients, relatives, and health care providers are aware of potential
cognitive and emotional problems after CA because both cognitive and emotional problems have significant impacts and can affect a patient's daily functioning, return to work, and quality of life.[19]

Spouse/caregiver
Not only the patients experience problems after the CA. Spouses and caregivers quite often feel highly burdened and have emotional problems, including symptoms of posttraumatic stress.[13,20] One of the changes that decreases the quality of life of spouses is the difficulty the patient has resuming his or her old life. The change of personality and behaviour and the need for lifestyle changes of the patient also may cause the partner stress.[10,21] Spouses feel the need for emotional support regarding partner relationships and regaining daily activities.[22]

Rehabilitation after OHCA: the missing link
As noted above, patients after CA often need both cardiac and cognitive rehabilitation. However, cardiac rehabilitation and cognitive rehabilitation most often are located in different teams and in different institutions.
In general, therapists at the cardiac wards have no experience in dealing with patients with cognitive deficits. Therapists might find these patients less trying, and patients seem to be unmotivated. Information has to be repeated regularly. There also seem to be more patients lost to follow-up when compared with myocardial infarction patients. Patients have difficulty picking up their lives, for example, when resuming work or in their relationship. Also, spouses become more protective and are afraid to leave the patient alone, afraid to let the patient perform certain activities, and afraid to participate in social events in fear of recurrence.[23]
On the other hand, cognitive rehabilitation therapists often see only

patients with very severe cognitive problems after a CA. This specific group of patients lacks insight into their deficits, which hampers cognitive rehabilitation. Patients with relatively mild cognitive deficits, who profit most from a cognitive rehabilitation intervention, are often not referred.[24] Even more important, cognitive therapists feel unsure about the physical training of the OHCA patients, especially the cardiopulmonary exercise capacity and possible limitations. In addition, patients who receive only cognitive rehabilitation receive no information on the psychological, social, and lifestyle factors as given in the regular cardiac rehabilitation programs.
Some patients receive both cardiac and cognitive rehabilitation. In that case, the advice may be contradictory and the amount of training may exceed the possibilities of the patient. The provided care is not centred around the patient.

Goal of rehabilitation after cardiac arrest
The goal of rehabilitation after CA is to provide excellent patient-centred cardiac and cognitive rehabilitation to all patients and their spouses/carers to achieve optimal participation in society, with minimal burden on spouses and society.
In 2011 in Leiden, The Netherlands, the Rijnlands Rehabilitation Centre developed a care path, "Rehabilitation after Resuscitation."

Integrated clinical care path
In this article we will outline the prerequisites as used in the care path, Rehabilitation after Resuscitation to develop a local clinical pathway to reach the above mentioned goal based upon the best available evidence. The main principles of the clinical pathway are:

- Adequate referral to rehabilitation for all patients after successful resuscitation
- Simple screening for cognitive impairments
- Screening for emotional problems
- Information on possible cognitive and emotional consequences to all patients and spouses
- Cardiac rehabilitation for all patients with cardiac cause of CA
- Cognitive rehabilitation when needed
- One integrated rehabilitation program
- Support and information to spouse, caregiver and/or family
- Aftercare

Adequate referral for all patients after successful resuscitation
All patients with a cardiac cause of CA should, according to international guidelines, be referred for cardiac rehabilitation.[7,9] The European Cardiac Rehabilitation Inventory Survey found that many patients are not adequately referred for cardiac rehabilitation.[25] Patients who have been resuscitated frequently follow more complex routes through the hospital due to multiple medical interventions in several departments. This results in an increased likelihood that survivors after CA are not adequately referred for rehabilitation. Considering the high incidence of cognitive impairments due to hypoxic brain injury after CA, we also argue that patients with a non-cardiac cause of CA should be referred for rehabilitation.
It is recommended to make strict referral agreements between local hospitals and the rehabilitation centre(s) in the area. The Rijnlands Rehabilitation Centre follows CA patients from the moment the ambulance service presents patients at the emergency department. A specialized nurse of the rehabilitation centre follows the patients throughout the hospital. This ensures that all eligible patients will get the opportunity to follow a rehabilitation program after discharge from the hospital. As soon as the patient is dismissed from the hospital, the rehabilitation process starts automatically.

Recommendation 1
Make referral agreements. Start following the CA-patients in an early hospital phase, so patients are not missed. Describe who is responsible for the referral to the rehabilitation centre.

Simple screening for cognitive impairments
Cognitive problems after OHCA are often mild. Extensive neuropsychological tests are able to detect mild cognitive problems. However, these assessments take approximately 3 hours, which makes them not suitable as a screening instrument for clinical daily practice. One could argue to use the Cerebral Performance Category (CPC), part of the Utstein Template, for screening.[26] The CPC is a classification system that roughly estimates the functioning of the patient at the time of hospital discharge. Torgersen et al showed that the CPC is not capable of detecting mild cognitive problems and therefore not suitable as a screening instrument.[27] A study by Cronberg et al used four perspectives in their study: clinician reported, performance measures,

observer reported, and patient reported. They concluded that subtle cognitive dysfunction can be missed when using clinician-reported measures (CPC and modified Rankin Scale).[28] At the moment, there is no uniformity as to which short cognitive screening would be best for this specific patient group. As long as no consensus is available, we advise the use of locally available screening instruments that measure at least aspects of memory, attention, and executive functioning. Some commonly used cognitive tests and questionnaires are described below.

The Montreal Cognitive Assessment

The Montrean Cognitive Assessment (MoCA) is a screening instrument for mild cognitive impairment.[29] It assesses attention and concentration, executive functions, memory, language, visuo-constructive skills, conceptual thinking, counting and orientation. The test takes approximately 10 minutes. The maximum score is 30. A score is considered deviant if < 26. In that case, further analysis should be considered. The MoCA showed already reasonable sensitivity and specificity in heart failure patients (64% and 66%, respectively).[30] The MoCA is freely available in many languages at http://www.mocatest.org. The test can be administered after a short instruction by almost all care providers. The interpretation of the results is preferably done by a health professional with expertise in the cognitive field.

The Mini-Mental State Examination

The Mini-Mental State Examination (MMSE) is a short, 11-item cognitive scale ranging from 0 to 30 points.[31] The test assesses multiple domains of cognitive functioning: orientation, memory, concentration, language and praxis. A cut off score of <28 indicates possible cognitive deficits. It takes ~10 minutes to conduct the MMSE. Unfortunately patients with minimal cognitive deficits score maximal due to a ceiling effect.[32] Therefore we have chosen only to use the MMSE when the MoCA is too difficult for the patient.

The Informant Questionnaire on Cognitive Decline of the Elderly

The Informant Questionnaire on Cognitive Decline of the Elderly (IQCODE), the only validated test for partners, is filled out by the spouse or other close relative to measure the patient's decline in cognitive functioning.[33] The survey compares the current cognitive functioning with past cognitive decline. For this group of patients, the functioning

before the CA is taken as a reference point. A score ≥ 3.6 indicates cognitive problems. When using the IQCODE, it is important to keep in mind that the outcome can be affected by the partners' mental state. A partner can feel worried or anxious after the CA. Therefore, they might give too much weight to the problems they experience. Another possibility is that cognitive impairments are not yet visible to the partner due to euphoria about the patient still being alive.

The Cognitive Failures Questionnaire

The Cognitive Failures Questionnaire (CFQ) is a self-reporting questionnaire that provides insight into the experienced cognitive problems of the patient.[20] The items relate to memory and attention. A score of > 32 indicates that the patient might have cognitive problems. However, the CFQ outcome should be handled with care. A low score might be related to lack of insight in the cognitive problems. A high score could be caused by worries for cognitive problems or depression instead of cognitive deficits. Therefore, we advise mainly to use the CFQ if there seems to be a discrepancy between the burden of the patient and the MoCA screening.

Recommendation 2

Screen all survivors for cognitive impairments. The MoCA is a simple and concise instrument for this purpose.

Screening for emotional problems

To assess emotional problems like depression, anxiety and PTSD the following questionnaires can be considered.

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report screening scale to indicate symptoms of anxiety and depression.[11] It is a short questionnaire and easy to use. The HADS contains two 7-item scales: one for anxiety and one for depression, both with a score range of 0 to 21. For the subscales, a score ≤ 7 signifies that it is unlikely that there is an anxiety disorder or a depression, and a score of 8 to 10 represents a possible anxiety disorder or depression. Scores of ≥ 11 indicate a definite anxiety disorder or depression.[11] Further assessment regarding an anxiety disorder or depression is needed when the patient scores ≥ 8 on the subscale(s).

Patient Health Questionnaire
In case of an positive depression score on the HADS, one can consider further exploration with the Patient Health Questionnaire (PHQ-9). The PHQ-9 is a multipurpose instrument to screen, monitor and measure the severity of depression.[34] A score of >5 indicates depression and further action is recommended: The higher the score, the more severe the depression.

Generalised Anxiety Disorder Assessment
In case of a positive anxiety score on the HADS, one can consider further exploration with the Generalized Anxiety Disorder Assessment (GAD-7). The GAD-7 is a self-administered patient questionnaire screening tool and severity measure for generalized anxiety disorder. [35] A score of >5 indicates more than average anxiety: The higher the score, the more severe the anxiety. When the score is ≥10, further evaluation is recommended.

Recommendation 3
Screen all survivors for emotional complaints. The HADS is one of the possible short and easy instruments for this purpose.

Information on cognitive and emotional consequences to patients and spouses
Patients and spouses are in need of information on the possible consequences of the CA.
Recently, an intervention called 'Stand still. . ., and move on' was developed by V. Moulaert which provides information on possible cognitive and emotional consequences after the CA. The intervention supports patients and their partners to promote self-management. It improves overall emotional state, anxiety, and quality of life; it also results in faster return to work.[36] The intervention is feasible and useful for patients and spouses.[37] The intervention can be given at the time of the screening.

The following items are addressed:
- Information on and explanation of possible cognitive problems
- Relationship between CA and lack of brain oxygenation
- Possible effect on cognition: forgetfulness, decreased concentration, mental slowness, difficulty following conversations (especially in

noisy places), and irritability
- Advice on how to deal with cognitive problems
- Information on other possible consequences for both
- patient and spouse
- Information about the normal process of emotional recovery of patient and caregiver
- Possible emotional changes (e.g., anxiety, depression)
- Physical and mental fatigue
- Advice on how to deal with emotional problems
- Fear of recurrence, dealing with death, fear for implantable cardioverter-defibrillator shocks (if relevant), social isolation
- Stress and burden of the caregiver
- Information about the rehabilitation care pathway
- Information about goals and possibilities at cardiac rehabilitation
- Information about goals and possibilities at cognitive rehabilitation

At the Rijnlands Rehabilitation Centre, the intervention is performed by a specialized nurse 4 weeks after patients are discharged from the hospital. During this visit, the screening is also performed. Instead of the specialized nurse, the intervention can also be performed by a physician assistant
or a therapist.

Recommendation 4
Provide information to all CA survivors on possible cognitive and emotional consequences in an early phase after dismissal from hospital.

Cardiac rehabilitation for all patients with cardiac cause of CA
Cardiac rehabilitation focuses on the physical, psychological, and social functioning of the patient after a cardiac event. Measures are also taken to prevent recurrence of (coronary) artery disease. Cardiac rehabilitation consists of coherent programs with comprehensive medical evaluations and prescribed exercises. Psychological counseling, information, and advice on lifestyle and coping are given to reduce the risk of sudden death or new infarcts. The rehabilitation starts during the hospital stay, and should be followed by a program during an outpatient phase over the next 3 to 6 months, followed by lifelong maintenance in which physical training and reduction of risk factors are integrated in daily life with or without (minimal) supervision.[5]

Cardiac rehabilitation has proven to have a positive effect on secondary prevention and mortality.[38] It also increases psychosocial well-being and return to work.[13,39]

Recommendation 5
Provide adequate cardiac rehabilitation for all patients with a cardiac cause of CA, aiming at optimization of physical condition and secondary prevention. Do not forget to provide this care for patients with cognitive impairments.

Cognitive rehabilitation when needed
For patients with acquired brain injury, cognitive rehabilitation has proven to be effective.[40] During cognitive rehabilitation, people learn in an interdisciplinary setting how to compensate for their cognitive impairments and how to use resources to retain optimal participation in society. Cognitive
rehabilitation also comprises psychoeducation to help patients and their families learn how to cope with the cognitive and emotional consequences of the brain injury.[41] There are no studies to date on the effectiveness of cognitive rehabilitation for patients with hypoxic brain injury due to CA. However, it is highly likely that OHCA survivors with cognitive deficits also benefit from cognitive rehabilitation interventions in the same way patients with other types of acquired brain injury do.

Recommendation 6
The threshold for referring CA survivors for neuropsychological assessment and cognitive rehabilitation programs should be low.

One integrated rehabilitation plan
To provide appropriate care tailored to patients' specific
situations, the care path (►Fig. 1), Rehabilitation after Resuscitation consists of three routes: Patients without cognitive problems start with regular cardiac rehabilitation. For patients who score below the cutoff on the cognitive screening, two possible routes can be followed. Patients with severe cognitive
problems (MoCA < 19) are advised to follow an individual cognitive rehabilitation program. The route of patients with mild cognitive

problems depends mainly on the desired level of participation and the support from (family) caregivers. The severity of the cognitive complaints and the nature of the request of help is leading. Quite often there is the need for further exploration of the cognitive complaints. These patients are offered a combined cardiac and cognitive rehabilitation program of the care path. At the Rijnlands Rehabilitation Centre, ~50% of the patients with mild cognitive complaints follow a more-extensive cognitive rehabilitation process.

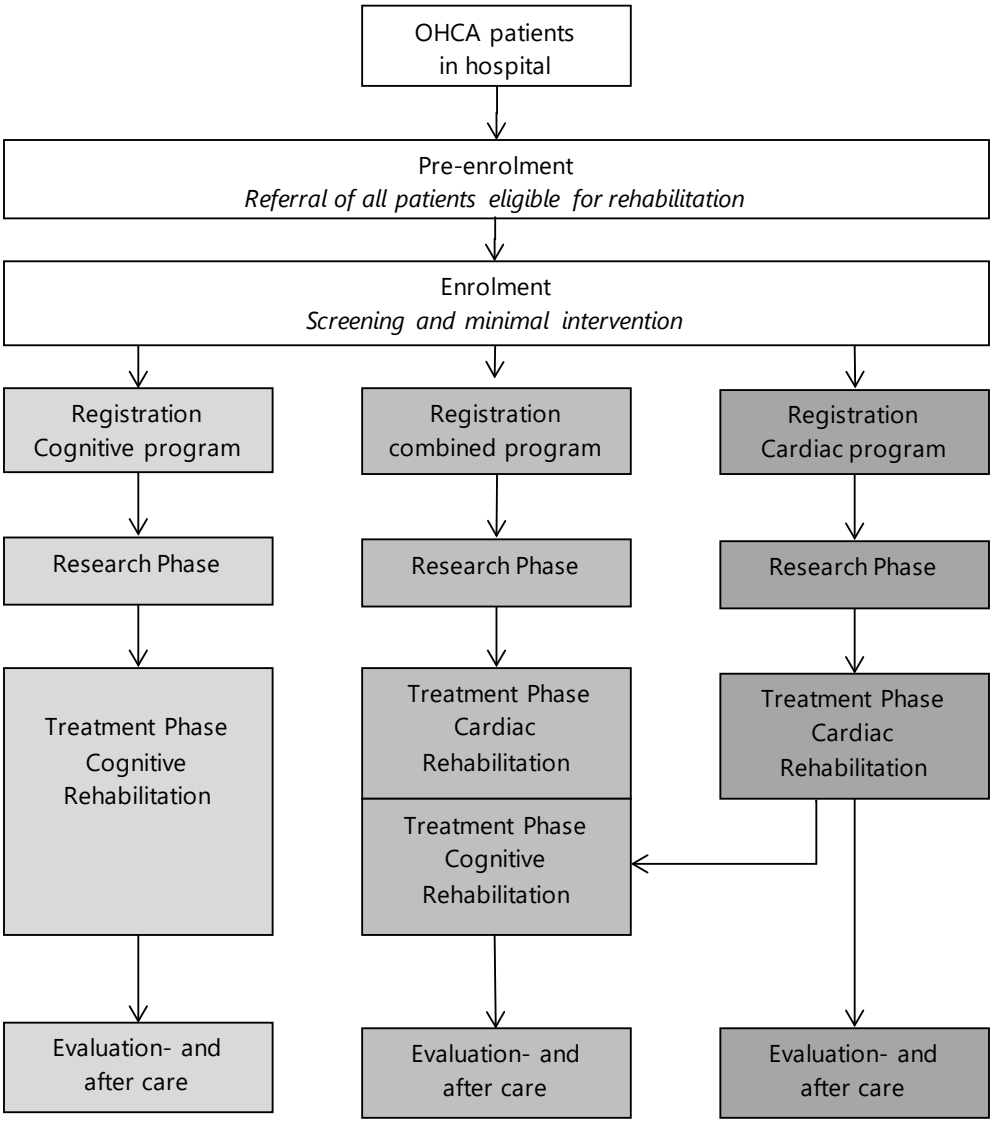

Fig 1 Care path of rehabilitation after resuscitation.
OHCA, out-of-hospital cardiac arrest.

Regular cardiac rehabilitation

Patients without cognitive complaints follow a cardiac rehabilitation program as recommended by international guidelines.[42–47] The core components of cardiac rehabilitation contain physical activity, health education, advice on cardiovascular risk reduction, and stress management.

Besides the cardiologist/physician, a physiotherapist, social worker, psychologist, and dietician are involved. Therapists should always be alert for symptoms of cognitive impairment. If any evidence of cognitive problems is detected during the cardiac rehabilitation process, a patient may be referred to a cognitive rehabilitation therapist for assessment. Additionally, the mental and emotional burden of the caregiver should be monitored more closely than for other patients in regular cardiac rehabilitation.

Individual cognitive rehabilitation

Patients with severe cognitive impairments start an individual rehabilitation program. The individual rehabilitation program is offered under the supervision of a rehabilitation specialist. The cardiologist, as consultant, gives advice on the cardiac training. The physiotherapist and rehabilitation physician of the cognitive rehabilitation ward should be aware of the training principles of cardiac rehabilitation.

Additionally, a neuropsychologist, social worker, and occupational therapist are part of the team. Individual goals are set in interdisciplinary team consultations depending on the need of the client and family and cognitive and physical possibilities.

The main goal of the therapy is to get the patient as independent as possible with optimal participation including social activities and return to work.

When possible and indicated, psychological, social, and lifestyle components of the cardiac rehabilitation program can be followed as part of the cardiologic rehabilitation department. If still needed, cardiac rehabilitation takes place after the cognitive rehabilitation.

Combined cardiac and cognitive rehabilitation

Patients with mild-to-moderate cognitive impairments follow a combined cardiac and cognitive rehabilitation program. They start with the cardiac rehabilitation program. Due to mild cognitive deficits, patients often suffer from sensory processing disorders. Therefore, we advise to offer the cardiac rehabilitation in a relatively small group (at the

Rijnlands Rehabilitation Centre, a maximum of eight patients), same staff every time, and low-volume level or no music. The physiotherapist from the cardiac rehabilitation team is trained to handle the consequences of cognitive problems. Near the end of the cardiac rehabilitation, an appointment is made with a cognitive rehabilitation specialist from the department of neurologic rehabilitation. On the basis of complaints and requests for help, the cognitive rehabilitation specialist assesses whether neuropsychological examination or cognitive rehabilitation is indicated.

Recommendation 7
Make both practical and formal agreements between cardiac and cognitive rehabilitation departments.

Support and information to spouse/family
After resuscitation, education about visible and invisible consequences of the CA is not only important for the patient, but also for relatives. This education begins during the screening for possible cognitive and emotional problems. During the cardiac and cognitive rehabilitation, specific attention needs to be paid to the spouse. We have had several instances in which spouses/family members experienced cardiac problems themselves in the period after the CA of the patient. Posttraumatic stress symptoms,
depression, and fear are common.[48] Often, supportive contact with a social worker is sufficient as intervention.
Sometimes, at the end of rehabilitation, the spouse still needs support. In The Netherlands, the Patient Partner Education Program 4All (PPEP4All) is offered for spouses of chronically diseased patients. This self-management program provides strategies for patients and spouses to manage the psychosocial consequences of the patient's disease from their own point of view. The program promotes the autonomy and self-reliance of both the patient and the spouse.[49]

Caregiver Strain Index
The Caregiver Strain Index (CSI) is a 13-item questionnaire designed to quickly identify partners with potential caregiving concerns. There is at least one item for each of the following major domains: employment, financial, physical, social, and time. Positive responses to seven or more items indicate a greater level of strain. The instrument can be used to

assess individuals of any age who are caregiver for an older adult.

Recommendation 8
Take care of the spouse and use CSI to identify concerns of the caregiver!

After care
Sometimes, cognitive and emotional complaints are not dominant in the sub acute phase, but arise (somewhat) later, for instance, when people return to work or when family circumstances change. Our clinical pathway showed that ~ 10% of the patients experience problems one year after the CA. We therefore recommend a short screening one year after the CA. A short conversation (by telephone) could be enough to detect issues. If present, an outpatient consultation of the rehabilitation physician can be scheduled.

Recommendation 9
Cognitive and emotional problems also may arise in a later stage after CA. Be aware of this and ask your patient.

Prerequisites
In order to make an excellent clinical rehabilitation pathway for CA patients, it is important to make good agreements, both in practical terms and at logistic/ administrative level, for example, cooperation agreements.

- Who initiates inclusion in the care path? Who screens for cognitive impairments and provides first information on possible cognitive and emotional consequences?
- Who decides in which route of the care path the patient starts?
- To offer an integrated rehabilitation care path, therapists of the cardiac rehabilitation need to have basic knowledge of cognitive problems. Reciprocally, therapists from the cognitive team need sufficient knowledge of cardiac training principles.
- Agreements on transfer between cardiac and cognitive rehabilitation departments are a prerequisite for success. Which information is transferred and by whom?

At the Rijnlands Rehabilitation Centre, we decided that every (para) medical therapist transfers information to his or her own counterpart. Of course, training results are also shared between teams.

Results of the integrated rehabilitation care path

In Leiden, 75% of all patients after OHCA are referred for cardiac rehabilitation. Patients who are not referred live in an institution or suffer from a severe comorbidity that hinders participation in rehabilitation. So we reached our first goal: adequate cardiac rehabilitation care for all resuscitated patients. Education was provided to all CA survivors and their family and a simple screening for cognitive problems was performed. Of the patients who were referred for cardiac rehabilitation, 23% experienced cognitive problems. One month after the OHCA, all patients experienced a lower QoL. For patients with cognitive impairments, the QoL was even worse.[50]

An inventory of patients' experiences with the care path was done by means of two focus groups performed according to guidelines for qualitative research. Both patients with and without cognitive complaints were satisfied with the content of the cognitive screening. Patients who did not show any

cognitive problems on the screening reported that they had more confidence in resuming everyday tasks and work.

Patients who showed possible cognitive complaints on the screening were offered an appointment with the cognitive rehabilitation physician. In approximately half of them, explanation and instructions by the rehabilitation physician were sufficient. In the other half, an extensive cognitive rehabilitation program was started.

Conclusions

It is essential to be aware of the high incidence of cognitive impairments in CA survivors. The MoCA seems to be a good screening instrument for cognitive impairments. The threshold for referring CA survivors for neuropsychological assessment should be low. Health care providers must be aware that
rehabilitation programs are available and can be of benefit for patients with cognitive impairments after CA. Local care chain arrangements aid in streamlining both referral to cardiac rehabilitation and from cardiac care to cognitive rehabilitation services.

Recommendation 10
When starting a local rehabilitation care path in your region, feel free to contact the authors.

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Chapter 6

Attention needed for cognitive problems in patients after out-of-hospital cardiac arrest: an inventory about daily rehabilitation care

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Abstract

Aim
Recent literature and Dutch guidelines for patients with out-of-hospital cardiac arrest OHCA) recommend screening for cognitive impairments and referral to cognitive rehabilitation when needed. The aim of this study is to assess the uptake of these recommendations for OHCA patients.

Method
An internet-based questionnaire was sent to 74 cardiologists and 143 rehabilitation specialists involved in rehabilitation of OHCA patients in the Netherlands. The questionnaire covered: background characteristics, availability and content of cognitive screening and rehabilitation, organisation of care, experienced need for an integrated care pathway including physical and cognitive rehabilitation, barriers and facilitators for an integrated care pathway.

Results
Forty-five questionnaires were returned (16 cardiologists and 29 rehabilitation doctors). Thirty-nine percent (n= 17) prescribed cognitive screening. Eighty-nine percent underscores an added value of an integrated care pathway. Barriers for an integrated care pathway included lack of knowledge, logistic obstacles, and poor cooperation between medical specialties.

Conclusions
In the Netherlands, only a minority of cardiologists and rehabilitation specialists routinely prescribe some form of cognitive screening in OHCA patients, although the majority underscores the value of cognitive screening in OHCA patients in an integrated care pathway. The uptake of such a care pathway seems hindered by lack of knowledge and organisational barriers.

Introduction

The majority of patients who survive an out-of-hospital cardiac arrest (OHCA) are eligible for cardiac rehabilitation due to the cardiac cause of the arrest [1–5]. Cardiac rehabilitation focusses on physical activity, health education and stress management [6]. However, cardiac rehabilitation does not address the highly prevalent cognitive problems that 45–52% of the OHCA survivors experience [7].

Most common cognitive problems in OHCA patients, due to hypoxic brain injury, are memory problems, attention deficits and executive problems [7]. Cognitive problems, however mild, can have a major impact on a person's participation/autonomy and quality of life and hamper good recovery [8]. Cognitive rehabilitation for patients with brain injury is proven effective [9].

In 1996, Grubb recommended paying attention towards cognitive problems after OHCA, subsequently emphasised by Moulaert in 2010 [10, 11]. Through the years guidelines also advised to screen for cognitive impairments and refer to cognitive rehabilitation when needed: the Dutch guidelines for cardiac rehabilitation of 2011 and the European Resuscitation Council (ERC) Guidelines for Resuscitation 2015 [5, 12–14]. One of the recommendations is to screen for cognitive impairments by using the Montreal Cognitive Assessment (MoCA) and to refer to a rehabilitation specialist if cognitive problems are found [12–14].

Additionally, the ERC mentions the use of the subjective Checklist for Cognition and Emotion as another possibility to identify possible cognitive symptoms. However, literature suggests that the use of subjective questionnaires merely discovers emotional problems [15]. Patients after OHCA frequently also suffer from emotional problems, such as anxiety (13–42%) and depression (8–45%) [16].

Emotional and cognitive symptoms often occur together and lead to poorer implementation of lifestyle changes and lower levels of participation [17]. A rehabilitation combination that covers both cardiac and neurological aspects seems the best option to reduce symptoms and improve patients' well-being [16, 18, 19].

This article aims to assess the uptake of the recommendations regarding cognitive screening and rehabilitation in OHCA survivors as described in literature and recent guidelines and to assess barriers and facilitators that influence the uptake of these recommendations for OHCA survivors. 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.

Materials and methods

Setting

A majority of the 79 hospitals in the Netherlands provides cardiac rehabilitation to low-risk patients, supervised by a cardiologist. Cardiac rehabilitation for high-risk patients and/or cognitive rehabilitation are provided in 35 specialised rehabilitation centres with in total 150 locations under supervision of a rehabilitation specialist. Twenty-nine locations provide both cognitive and cardiac rehabilitation, 33 locations provide only cognitive rehabilitation and 6 provide only cardiac rehabilitation.

Study design

In May 2015, an internet-based questionnaire was sent to rehabilitation specialists and cardiologists in Dutch rehabilitation centres and hospitals that provide cardiac and/or cognitive rehabilitation. Since most rehabilitation centres and hospitals were staffed with several medical specialists, multiple questionnaires were sent to each location. Reminders were sent two months later. The questionnaire consisted of open-ended, multiple choice or multi response questions. Questionnaires were returned anonymously.

Study population

Cardiologists

Locations providing cardiac rehabilitation were retrieved by an internet search. Cardiologists registered with the Netherlands Society of Cardiology (Nederlandse Vereniging voor Cardiologie—NVVC) and the Dutch multidisciplinary consultative body on cardiac rehabilitation (Landelijk Multidisciplinair Overleg Hartrevalidatie—LMDO-H) were invited. Locations without a member of the Netherlands Society of Cardiology were invited to participate via a general email address. In total, 74 cardiologists were invited.

Rehabilitation specialists

All rehabilitation centres and locations were found via the website of Revalidatie Nederland, the Dutch branch organisation for

rehabilitation centres. Cognitive rehabilitation specialists were traced via the Werkgroep CVA Nederland (WCN), a national workgroup on the rehabilitation of stroke patients. Locations not represented in the task force were invited to participate via a general email address. In total, 143 rehabilitation specialists were invited.

Questionnaire

The questionnaire was based on review of literature and available guidelines [7, 19, 20]. Barriers were explored based upon the framework of Grol and Wensing, which categorises barriers and facilitators for the uptake of innovations into five levels: characteristics of the innovation, the individual professional, the individual patient, social context, organisational context and economic & political context [21]. During the development of the questionnaire, three semi-structured telephone interviews were conducted (a cardiologist and a rehabilitation specialist from a rehabilitation centre and a hospital cardiologist) to explore the barriers and facilitators for the uptake of the recommendations regarding cognitive screening, as input for the questions of the questionnaire.

The questionnaire included 30 questions about: (1) background characteristics (age, gender, institution [hospital, rehabilitation centre], work experience [years], number of OHCA patients per year [number of patients]); (2) availability and content of cognitive screening (patient routinely screened for cognitive problems [yes/no] and if not available, how are cognitive problems detected [intake, neuropsychological assessment, observation by team], what is the content of screening [objective, subjective], who is responsible for screening [cardiologist, rehabilitation specialist, psychologist, specialised nurse/physician assistant, paramedic], and what are the policies used when cognitive problems were suspected [intake psychologist, intake social worker, start cognitive rehabilitation, other]); and (3) experienced need for integrated care pathway in which cognitive screening is included [yes/no], existing barriers and facilitators for an integrated care pathway (awareness cognitive problems, logistic factors, factors regarding population, effects for patients [yes/no]).

Analysis

We used descriptive statistics to analyse the data gathered by the questionnaire. The interviews were analysed qualitatively. However, the data from the interviews were only used to develop our questionnaire. We did not report the results of the interviews in our manuscript. The descriptive statistics were used for characteristics and current care for all respondents and for cardiologists or rehabilitation specialists separately. Chi-square tests, Mann-Whitney U tests and unpaired t-tests (SPSS 22 v.02) were used to test differences between groups where appropriate. In case of expected cell count less than five, Fisher's exact test was used. P-values ≤ 0.05 were considered statistically significant.

Results

Characteristics of respondents

The characteristics of respondents are shown in Table 1. A total of 45 respondents completed the questionnaire (21% response rate). The median age of respondents was 42 years (range 31–61), the majority (n= 16) had 5–10 years working experience with OHCA patients and saw 0–10 OHCA patients per year (n= 18). Fifty-three percent (n= 24) worked in a hospital, 42% (n= 19) in a rehabilitation centre and 5% (n= 2) in both.

Table 1 Characteristics of respondents on a questionnaire on care OHCA
CR cardiac Rehabilitation OHCA Out-of-hospital cardiac arrest PA=Physician Assistant,

	Total respondents	**cardiologists**	**rehabilitation specialists**
	n=45	n=16	n=29
Age (median, range)	42 (31-61)	38 (31-59)	44 (31-61)
years of clinical experience with OHCA			
1-5	11 (24%)	4 (25%)	7 (24%)
5-10	16 (36%)	8 (50%)	8 (28%)
10-15	8 (18%)	1 (6%)	7 (24%)
> 15	10 (22%)	3 (19%)	7 (24%)
Institution			
hospital	24 (53%)	9 (56%)	15 (52%)
rehabilitation centre	19 (42%)	6 (38%)	13 (45%)
hospital and rehabilitation centre	2 (5%)	1 (6%)	1 (3%)
Estimated number of OHCA patients seen per year [a]			
0-10	18 (40%)	4 (25%)	14 (48%)
10-20	10 (19%)	1 (6%)	9 (31%)
20-30	4 (9%)	3 (19%)	1 (3%)
>30	10 (22%)	7 (44%)	3 (10%)
unknown	3 (7%)	1 (6%)	2 (7%)

GP=General Practitioner
a p-value ≤0.05 * more than one answer possible

Availability and content of cognitive screening and rehabilitation

Table 2 shows the availability and content of cognitive screening and rehabilitation.

Of the 45 respondents 39% (n= 17) reported they used a standard cognitive screening in OHCA patients. Of these 17 respondents, 65% (n= 11) used an objective measurement: MoCA, Mini Mental State Examination (MMSE) or neuropsychological assessment.
Subjective methods are used by 35% (n= 6). A standardised questionnaire used by 2 of these respondents is the Cognitive Failures Questionnaire (CFQ). Cardiologists more often use a subjective screening (50%, n= 3) than rehabilitation specialists (27%, n= 3).

Cardiologists who reported using a screening, delegate this task to other health professionals. The majority of respondents who do not screen routinely rely on the observations during intake (41%, n= 11) or by their teams (54%, n= 14). In the absence of standard cognitive screening, cardiologists (90%, n= 9) use a non-structured observation,

whereas rehabilitation specialists (59%, n= 10) refer patients to a cognitive rehabilitation team.
Respondents who screen for cognitive problems refer, when needed, to cognitive rehabilitation (71%, n= 12), psychologist (24%, n= 4) or social worker (18% n= 3).

Most respondents (68%, n= 30) find it is easy to refer from cardiac to cognitive rehabilitation in case of cognitive problems. Twenty percent has close collaborations in either a pathway (11%) or cardiac and cognitive rehabilitation within the same team (9%).

Table 2 Availability and content cognitive screening and rehabilitation for OHCA patients

	N (%)	**cardiologists**	**rehabilitation specialists**
Screening (n=44)		n=16	n=28
yes	17 (39%)	6 (37%)	11 (39%)
no	27 (61%)	10 (63%)	17 (61%)
Content screening (n=17)*		n=6	n=11
objective screening	11(65%)	4 (67%)	7 (64%)
subjective screening	6 (35%)	3 (50%)	3 (27%)
Who assesses screening (n=17)*		n=6	n=11
cardiologist	0 (0%)	0 (0%)	0 (0%)
rehabilitation specialist	5 (29%)	0 (0%)	5 (45%)
psychologist	6 (35%)	1 (17%)	5 (45%)
specialised nurse/physician assistant	5 (30%)	4 (67%)	1 (9%)
paramedic	4 (24%)	1 (17%)	3 (27%)
other	1 (6%)	1 (17%)	0 (0%)
Assessment cognitive problems by lack cognitive screening*		n=10	n=17
intake for cognitive rehabilitation	11 (41%)	1 (10%)	10 (59%)
neuropsychological assessment	2 (8%)	0 (0%)	2 (12%)
observation of cognitive problems by team	14 (54%)	9 (90%)	5 (29%)
other	3 (12%)	0 (0%)	3 (18%)
Action if possible cognitive problems (n=17)*		n=6	n=11
intake psychologist	4 (24%)	1 (17%)	3 (27%)
intake social worker	3 (18%)	3 (50%)	0 (0%)
start cognitive rehabilitation	12 (71%)	3 (50%)	9 (82%)
other	1 (6%)	0 (0%)	1 (9%)
Cooperation cardiac and cognitive rehabilitation (n=44)		n=16	n=28
care pathway/co-operative agreements	5 (11%)	3 (19%)	2 (7%)
cardiac and cognitive rehabilitation in same team	4 (9%)	2 (13%)	2 (7%)
easy referral from cardiac to cognitive rehabilitation	30 (68%)	11 (69%)	19 (68%)
NA/unknown	5 (11%)	0 (0%)	5 (18%)

A not available, OHCA out-of-hospital cardiac arrest
*more than one answer possible

Experienced need for an integrated care pathway and barriers and facilitators

Almost all respondents (89%, n= 39) see an added value in an integrated care pathway for OHCA patients (Tab. 3 *next page*).

One of the barriers mentioned for a care pathway is lack of knowledge of specialists regarding cognitive problems. However, most respondents are aware of memory problems (87%, n= 39), attention deficits (76%, n= 34), problems in reintegration in work (71%, n= 32) and relational problems (51%, n= 23). No major differences were found regarding awareness between responding cardiologists and rehabilitation specialists. Nevertheless, eight rehabilitation specialists (31%) mentioned a lack of knowledge regarding cognitive problems by cardiologists. Organisational barriers that hamper the implementation of a care pathway are logistic problems (44%, n= 17), difficulties in cooperation between cardiac and cognitive rehabilitation 36% (n= 14) and the small number of patients 36% (n= 14). In addition, 21% (n= 8) of the respondents fears an increase of administrative load and one person (3%) mentioned not achieving production agreements as a financial barrier.

An opportunity is seen in the organisational facilitator of already existing co-operations between departments (89%). The majority (89%) sees an added value in a care pathway or co-operative agreement. Most respondents also see opportunities in better alignment of cardiac and cognitive rehabilitation (71%, n= 32), more focus on patients' needs (61%, n= 25), fewer chances of relapse (56%, n= 23) and less dropouts during the cardiac rehabilitation programme (2%, n= 1).

Table 3 Barriers and facilitators for an integrated care pathway

		n (%)	cardiologists	rehabilitation specialists
BARRIERS				
Knowledge		n=42	n=16	n=26
Lack of knowledge of cognitive problems by specialists for accurate referral		8 (21%)	0 (0%)	8 (31%)
Awareness cognitive impairment		n=45	n=16	n=29
Functioning	Memory problems	39 (87%)	14 (88%)	25 (86%)
	Attention deficits	34 (76%)	12 (75%)	22 (76%)
	Executive problems	16 (36%)	2 (13%)	14 (48%)
Activity	Decision making	12 (27%)	5 (31%)	7 (24%)
	Manage calendar	11 (24%)	3 (19%)	8 (28%)
	Make shopping list	4 (8%)	2 (13%)	2 (7%)
	Cleaning/running household	8 (18%)	3 (19%)	5 (17%)
Participation	Problems reintegration work	32 (71%)	13 (81%)	19 (66%)
	Relational problems	23 (51%)	10 (63%)	13 (45%)
	Safety	11 (24%)	1 (6%)	10 (34%)
	Attending traffic	10 (22%)	2 (13%)	8 (28%)
Other		6 (13%)	2 (13%)	4 (14%)

Organisational	n=42	n=16	n=26
Logistic problems	17 (44%)	5 (31%)	12 (46%)
Increase administrative load	8 (21%)	5 (31%)	3 (12%)
Patient population too small	14 (36%)	6 (38%)	8 (31%)
Difficulty cooperation departments	14 (36%)	3 (19%)	11 (42%)
Financial	n=42	n=16	n=26
Not achieving production agreements	1 (3%)	1 (6%)	0 (0%)
FACILITATORS			
Organisational			
Existing cooperation between departments	n=44	n=16	n=28
Care pathway /co-operative agreements	5 (7%)	3 (19%)	2 (7%)
Cardiac and cognitive rehabilitation in same team	4 (9%)	2 (13%)	2 (7%)
Easy referral cardiac to cognitive rehabilitation	30 (50%)	11 (69%)	19 (68%)
NA/unknown	5 (11%)	0 (0%)	5 (18%)
Added value care pathway/co-operative agreement			
Yes	39 (89%)	15 (94%)	24 (86%)
No	5 (11%)	1 (6%)	4 (14%)
Innovation	n=44	n=15	n=29
Care cardiac / neurorehabilitation better aligned	32 (78%)	10 (67%)	22 (76%)
Less drop outs cardiac rehab	1 (2%)	1 (7%)	0 (0%)
Less chance relapse	23 (56%)	9 (60%)	14 (48%)
Better alignment help request patient	25 (61%)	7 (47%)	18 (62%)

Discussion

This study describes that both cardiologists and rehabilitation physicians in the Netherlands pay attention to cognitive problems in OHCA patients. The uptake of the recommendations to assess cognitive problems in OHCA survivors is poor though and needs improvement. Although all respondents in this study mention they use some sort of screening, only 39% of the respondents routinely use a standardised screening for cognitive problems in OHCA patients and a mere 25% use a standardised objective screening.

Two objective screening tools are used by a small amount of respondents—MoCA and MMSE. The MoCA, which only takes 10min, measures memory, visuospatial abilities, executive functions, attention, concentration and orientation of the cognitive impairment spectrum, and with a sensitivity of 90% and specificity of 87% it is the best short screening available at the moment [22, 23].

The ERC resuscitation guidelines also recommend MoCA and advise referral to a neuropsychologist or rehabilitation specialist if signs and symptoms of cognitive impairments are found.

Subjective instruments (based upon patients' own point of view) are also recommended in the ERC resuscitation guidelines. The Cognitive Failures Questionnaire (CFQ) is such an instrument and is used by some of the respondents who routinely screen for cognitive problems. The CFQ, a questionnaire about cognitive mistakes, is not specifically recommended in the ERC guidelines but is similar to the recommended Checklist Cognition and Emotion. Literature suggests that the use of the CFQ might not reveal cognitive deficits but merely emotional problems, and should therefore rather be used complementary to the objective screening for cognitive problems [15].

Respondents who do not standardly screen (61%) indicate that they assess cognitive problems using non-structured observations by the team. Patients they suspect of cognitive problems are referred for cognitive rehabilitation or neuropsychological assessment. It is well known that non-structured observations lead to false-negative results that can be avoided by using either structured observations or screenings [22].

The lack of treatment protocols for both screening and treatment of cognitive deficits after OHCA is striking, given the recommendations in the guidelines.

Cognitive rehabilitation has proven to be effective for patients with acquired brain injury [9]. Cognitive rehabilitation teaches people how to compensate for cognitive impairments and how to use resources to retain optimal participation in society. Psycho-education is offered to help the patient and the family learns how to cope with cognitive and emotional consequences of brain injury [24]. Although no studies are available on the effectiveness of cognitive rehabilitation for patients with hypoxic brain injury due to cardiac arrest, it is likely that OHCA survivors with cognitive impairments benefit from cognitive rehabilitation interventions in the same way patients with other types of acquired brain injury do [9, 20].

A positive aspect towards future treatment protocols is that all specialists are aware of one or more possible cognitive problems. The majority of the respondents sees an added value in an integrated care pathway resulting in better alignment of care, better fulfilment of the patient's needs and decrease of the chance of relapse. Since the vast majority (89%) already has an existing co-operation between departments, rapid implementation of the recommendations should be possible.

However, logistic barriers and lack of structural cooperation between cardiac and cognitive rehabilitation hamper the uptake of these recommendations. Specialists also fear an increase of administrative load for a small population.

Strengths and limitations

We extensively approached specialists involved in care for OHCA patients. By doing so, multiple specialists at one location were approached. Often only one of them reacted, explaining the low response rate. Probably, this introduces a selection bias with overrepresentation of specialists interested in cognitive problems.

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Chapter 7

Out-of-hospital cardiac arrest survivors need both cardiological and neurological rehabilitation!

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Abstract

Purpose of review

Most survivors of out-of-hospital cardiac arrest (OHCA) suffer from cardiologic symptoms and approximately half of them experience cognitive problems because of hypoxic brain damage. Symptoms of anxiety and depression are also common. This review aims to give an overview of recent literature on rehabilitation treatment aiming at improvement of quality of life after OHCA.

Recent findings

Existing cognitive screening tools are now validated for OHCA survivors. OHCA patients with cognitive deficits may have lower exercise capacity. Cardiac rehabilitation seems to be well tolerated for OHCA survivors, with outcomes comparable to myocardial infarction patients. Many caregivers suffer from
posttraumatic stress disorder and emotional stress. Interventions for them are available. Implementation of integrated programs covering both cognitive and cardiac rehabilitation is hampered by lack of knowledge and organizational barriers.

Summary

OHCA survivors should be routinely screened for cognitive and emotional problems. When patients with mild cognitive deficits participate in cardiac rehabilitation, their program should be adjusted to their cognitive abilities. For patients with severe cognitive or emotional problems, individualized rehabilitation seems favorable. Integrated rehabilitation treatment between cardiac and cognitive rehabilitation departments is recommended. Attention should be paid to the burden of caregivers.

Introduction

With the improvements made in the chain of survival, survival rates after out-of-hospital cardiac
arrest (OHCA) have increased and are expected to increase even more, for example, by creating citizen responder networks [1–3]. Survivors of OHCA suffer from sequelae of physical, cognitive, and emotional consequences. Approximately half of them experience cognitive problems and even more survivors experience symptoms of anxiety, depression, or posttraumatic stress [4–7]. These impairments have serious impact on daily functioning, societal participation, and quality of life [8**,9,10]. Therefore, it is crucial not only to focus on survival but also pay attention to the long-term outcome of survivors.

'Individuals surviving OHCA are at high risk of long-term cognitive impairment and mental health issues with a negative impact on participation and quality of life.'

Cardiac rehabilitation after outof-hospital cardiac arrest

In most cases, OHCA is of cardiogenic cause and therefore patients should follow cardiac rehabilitation [11]. Cardiac rehabilitation programs traditionally focus on education aimed at a healthy lifestyle and improvement of exercise capacity with the goal of returning to 'normal' life [12]. One study described a negative correlation between cognitive impairments and exercise capacity after OHCA [13]. Unfortunately, there is little research investigating cardiac rehabilitation specifically for the OHCA population. But cardiac rehabilitation for OHCA survivors seems to be well tolerated and the outcomes comparable to cardiac rehabilitation after myocardial infarction [14].

For cardiac patients with mild-to-moderate physical deficits without additional problems, online or telephone cardiac rehabilitation seems to be as effective as and more cost-efficient than center-based programs [15]. However, OHCA survivors specifically have experienced a tumultuous and life-changing event. Fear, anxiety, loss of memory, and difficulty adjusting to a new reality, both in
relationships with other people, as well as in the relationship with their own body, are part of their experiences. The presence of anxiety and depression do not only negatively influence quality of life but also known to increase the risk of new cardiac events and mortality [16].

OHCA survivors may need a more holistic pathway, focusing on both physiological and psychological function [17**].
Attention is also needed for spouses and caregivers that do not feel well supported in cardiac programs [17**]. They often show symptoms of anxiety, depression, and posttraumatic stress because of the witnessed arrest, the bystander cardiopulmonary resuscitation, and the long intensive care unit stay [18]. Cardiac patients and spouses have unmet education needs following an acute cardiac event and information increases control and decreases negative emotions associated with diagnosis [19*]. Cardio pulmonary resuscitation (CPR) training for spouses may also be useful to diminish fear [19*]. 'After an OHCA, patients and spouses need psychosocial and emotional support as part of cardiac rehabilitation.'

Screening

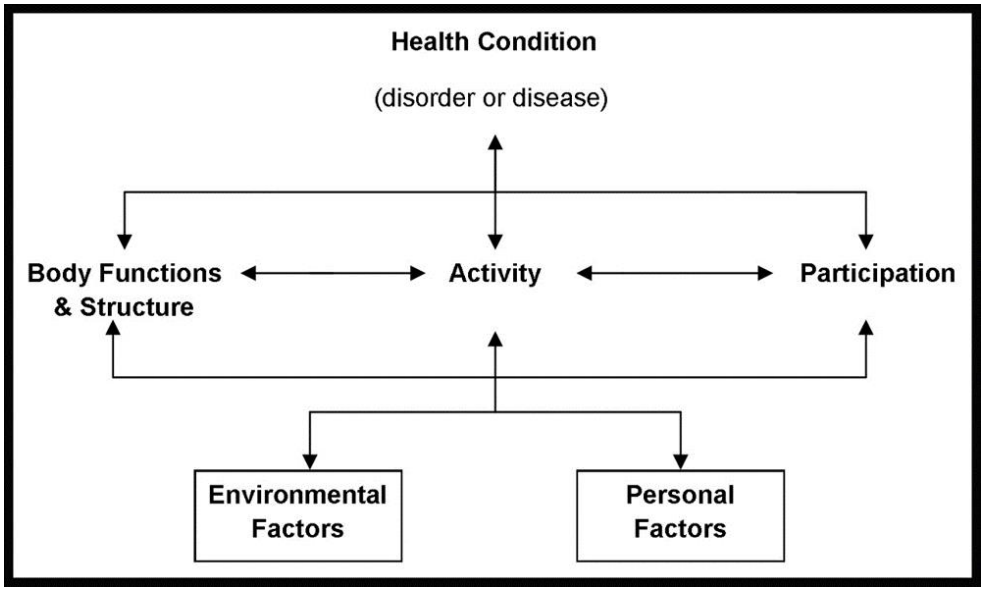
When assessing outcome of cardiac arrest, studies have traditionally focused on survival rates and relatively short-term clinician-based assessments. The Utstein-style guidelines recommend using the 5-point Cerebral Performance Category (CPC) scale to assess neurological outcome after cardiac arrest [20]. Patients with CPC scores of 3 or higher are commonly regarded as having 'poor' outcome. Patients with CPC 1, able to return to normal activities, and CPC 2, able to live independently, are regarded as good outcomes. Studies using the CPC have suggested that the majority of cardiac arrest survivors have a good neurological outcome [21]. However, half of the patients with a CPC of 1 or 2 experience problems in cognition or emotional wellbeing that were not identified using the CPC [22*]. On neuropsychological tests, deficits of attention, declarative memory, executive function, visuospatial abilities, and verbal fluency are found [7]. In daily practice, it is not possible to administer neuropsychological tests to all survivors. The Montreal Cognitive Assessment (MoCA) – a cognitive screening instrument – seems to have good correlation to the Computer Assessment of mild cognitive impairment in patients surviving cardiac arrest [23*]. The MoCA can be administered by regular hospital staff and takes approximately 10 min. When it is not possible to administer an objective screening, a questionnaire asking the caregiver may provide better information than asking the patient himself [24]. To screen for emotional problems, the Hospital Anxiety and Depression Scale (HADS), that covers both anxiety and depressive symptoms, seems to be a useful questionnaire [22*].

'Screening for cognitive and emotional impairments after OHCA is highly recommended. The MoCA seems to be a sensitive cognitive screening tool for this purpose. The HADS is recommended to screen for emotional problems.'

Cognitive rehabilitation after outof-hospital cardiac arrest

Cognitive rehabilitation focuses on the consequences of the cognitive impairments on the 'activity and participation' level on the basis of the International Classification of Functioning, Disability, and Health of the World Health Organization (Fig. 1) [25].

Figure 1. The International Classification of Functioning, Disability, and Health model.



The rehabilitation physician and his team determine the health consequences of the OHCA across all domains of functioning and take the desired level of activity and participation of the patient into account. This leads to a treatment plan that teaches the patient and their families compensatory techniques to recognize, live with, manage,

bypass, reduce, or come to terms with cognitive deficits [26].
Most rehabilitation teams that are specialized in cognitive rehabilitation, however, have limited knowledge of cardiac rehabilitation and vice versa. Cooperation between cardiological and neurological rehabilitation teams is needed to provide patients a holistic treatment program that covers all sequelae of their cardiac arrest [17**].

'Cooperation between cardiological and neurological rehabilitation teams is needed in case of cognitive consequences.'

Integrated rehabilitation care path

In the Netherlands, both cardiac and cognitive rehabilitation teams are available throughout the country, covered by insurance companies and thus easily accessible for patients. A large majority (89%) of healthcare providers involved in care for OHCA patients support the idea of a combined cardiac and cognitive program after cardiac arrest. However, this same survey showed that cognitive and emotional screening tools are not taken out routinely and not all patients are offered cardiac rehabilitation [27].
There are few articles exploring interventions focused on improving quality of life for survivors of CA. Hence, the effectiveness of these programs is not well known. A concise intervention that consists of screening for cognitive and emotional problems and provision of information has been developed and seems clinically feasible and cost-effective [28].
It seems sensible to refer patients with more severe cognitive problems to an individualized cognitive rehabilitation program with involvement of a cardiologist for exercise training advice. Patients
with mild-to-moderate cognitive problems will probably benefit from a cardiac rehabilitation program that takes into account cognitive problems. Smaller training groups, less distracting stimuli, for example, loud music, and avoidance of dual tasks may be necessary. This implies that cardiac training personnel should at least have some knowledge of cognitive training principles. During the cardiac rehabilitation, a meeting with a cognitive rehabilitation specialist or psychologist can be scheduled to decide whether a cognitive rehabilitation trajectory is needed. A program covering these aspects has been developed in the Netherlands [29].

Conclusion

All OHCA survivors should be routinely screened for cognitive and emotional problems. The objective MoCA test seems well suited for this purpose. When it is not possible to administer the MoCA, a questionnaire for family or caregivers can be considered. To screen for emotional problems, the HADS is a useful questionnaire. Patients with cognitive deficits after OHCA may have a lower exercise capacity. Their rehabilitation program should be adjusted to their cognitive abilities. Emotional support should be offered to the patients and their caregivers. For patients with severe cognitive deficits, individualized cognitive rehabilitation is needed that focuses on compensation strategies to reach maximal participation. Also in patients with cognitive deficits, expertise in cardiology is needed to design a proper training schedule. Therefore, cooperation is needed between cardiac and cognitive rehabilitation specialties.

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Conflicts of interest
There are no conflicts of interest.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted
as: * of special interest ** of outstanding interest

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Chapter 8

Summary and General discussion

Summary

This thesis describes how to optimise the rehabilitation care for patients after an out-of-hospital cardiac arrest (OHCA), in particular by taking cognitive problems into account.

The general introduction, **Chapter 1**, includes the definition, epidemiology and survival rates of OHCA and provides a brief history of resuscitation. In addition, the chain of survival is explained: a model that describes the different steps needed to optimise the chance of survival for patients after an OHCA.
When patients survive an OHCA many of them have to cope with the consequences of hypoxic ischemic brain injury caused by the cardiac arrest. Especially cognitive problems may have a major impact on a patient's life, and thus need to be taken into account during rehabilitation treatment.

To provide more insight into survival after an OHCA, **Chapter 2** describes the survival rates in an optimised chain of survival in the region Leiden. This retrospective cohort study describes 242 patients who were treated by the Emergency Medical Service and were resuscitated between April 2011 and December 2012. In 76% of the patient the cardiac arrest (CA) was of cardiac origin and 52% of the treated patients had a shockable rhythm when the Emergency Medical Service arrived. Seventy-four percent of the CA's were witnessed and 76% of the patients had received bystander cardio pulmonary resuscitation. In 39% an automated external defibrillator was used during the resuscitation. Of the 242 patients, 74 (31%) died on the emergency ward. Of the 168 hospitalised patients, 144 (86%) underwent (sub) acute therapeutic procedures like Coronary Artery Bypass Grafting (CABG), Percutaneous Coronary Intervention (PCI), Temperature Target Management (TTM) or an implantable cardioverter defibrillator (ICD). 105 patients (43%) were discharged alive. Factors that were statistically significantly associated with survival until discharge were younger age, CA in a public area, a witnessed CA, cardiac origin with shockable rhythm, the use of an AED, shorter time until return of spontaneous circulation and a Glasgow Coma Scale (GCS) ≥13 during transport by the ambulance.

Some patients eligible for cardiac rehabilitation after OHCA may encounter cognitive problems. **Chapter 3** describes a prospective

cohort study in 77 OHCA patients referred for cardiac rehabilitation in a rehabilitation centre between February 2011 and February 2013. Screening for cognitive problems included the objective Mini-Mental State Exam (MMSE), whereas subjective cognitive problems experienced by the patient and the spouse or caregiver were measured with the Cognitive Failures Questionnaire (CFQ) and the Informant Questionnaire on Cognitive Decline of the Elderly (IQCODE).
Combining the results of the objective test and the subjective questionnaires, 23% of the participants had cognitive problems (10% according to the MMSE and 13% according to the CFQ and/or IQCODE). A negative correlation was found between cognitive problems and quality of life as measured with the Impact on Participation and Autonomy Questionnaire (IPAQ) and the SF-36 Health Survey.

Whereas the association between cognitive problems and overall quality of life is well established, little is known on the relationship between cognitive problems and physical health, in particular exercise capacity. Therefore in **Chapter 4**, a retrospective study on the exercise capacity of OHCA survivors with and without cognitive problems is described. In order to compare homogeneous groups, only patients with OHCA caused by a myocardial infarction were included in this study. Of 53 patients cardiopulmonary exercise test data were available. Nine of them (17%) had cognitive problems according to MMSE, CFQ and IQCODE. Statistically significant differences between patients with and without cognitive impairments were observed for VO2peak (median 14.5 vs 19.7 ml/kg/min), workload (median 130.0 vs 143.5 W) and MET's (median 4.1 vs 5.6).
Although the study was small, there seems to be a negative correlation between cognitive impairments and exercise capacity in patients referred for rehabilitation after OHCA caused by myocardial infarction. This finding underlines the need for a cardiac work-up in patients with cognitive problems after OHCA.

Most patients need cardiac rehabilitation after OHCA, but with this rehabilitation, attention needs to be paid towards possible cognitive problems. **Chapter 5** describes an integrated clinical care pathway for patient-centred rehabilitation care after a cardiac arrest, aiming at the optimisation of participation in society. For that purpose, both cardiac and cognitive rehabilitation processes need to be coordinated. Ten main principles that constitute the basis of the care pathway are

discussed, derived from the best available evidence. Most important is that all survivors need a timely referral to a rehabilitation program. For all patients with a cardiac cause of the CA this program should contain cardiac rehabilitation. Patients need to be screened for cognitive and emotional problems. If needed, patients should be referred for cognitive rehabilitation. The rehabilitation includes the provision of information to patients and spouses, not only on physical but also on possible cognitive and emotional consequences of the OHCA. In particular attention should be paid towards spouses, as they are often anxious and concerned, which may hamper recovery and return to society of the patient.

Regarding the extent to which practice recommendations and guidelines are actually followed in the Netherlands, a cross-sectional study is presented in **Chapter 6**. It concerned an internet-based questionnaire on the uptake of the recommendations to screen for cognitive impairments and refer survivors of an OHCA to cognitive rehabilitation when needed, as recommended by literature and Dutch guidelines. The questionnaire was distributed to specialists known to be involved in the rehabilitation of OHCA patients in The Netherlands, i.e. 74 cardiologists and 143 rehabilitation specialists. Topics covered by the questionnaire were: background characteristics of the respondent, availability and content of cognitive screening and rehabilitation in their region, organisation of care, perceived need for an integrated care pathway including physical and cognitive rehabilitation, barriers and facilitators for an integrated care pathway. Forty-five questionnaires were returned (16 cardiologists and 29 rehabilitation specialists). A majority of the participants (89%) underscored the value of a cognitive screening in OHCA patients in an integrated care pathway. Seventeen (39%) reported to prescribe some form of cognitive screening, but only 25% used an objective measurement instrument to identify cognitive problems. Perceived barriers for the implementation of an integrated care pathway included lack of knowledge, logistic obstacles and poor cooperation between medical specialities.
This study showed that only a minority of the cardiologists and rehabilitation specialists in the Netherlands routinely use some form of cognitive screening in OHCA patients. The uptake of an integrated care pathway seems hindered by lack of knowledge and organisational barriers.

Chapter 7 gives an overview of recent literature on rehabilitation treatment after OHCA. International consensus exists that OHCA-survivors need integrated treatment, covering both cardiologic and neurologic aspects of rehabilitation. In order to routinely screen for cognitive and/or emotional problems, the objective MoCA test and the Hospital Anxiety and Depression Score (HADS) seem most appropriate. Cardiac rehabilitation after OHCA appears to be as effective and safe as in other patient groups. It should be noted however, that patients with cognitive problems may have a lower exercise capacity. Their rehabilitation program should be adjusted to both their cognitive and cardiac abilities. Individualised cognitive rehabilitation is needed for patients with severe cognitive deficits to teach them compensation strategies in order to reach maximal participation. Emotional support should be offered to both patients and their spouses/caregivers. It is concluded that both cardiac and cognitive rehabilitation expertise is needed and should be integrated to provide appropriate rehabilitative care to OHCA survivors.

General discussion

An out-of-hospital cardiac arrest (OHCA) is a major unexpected life threatening event. Survival rates are slowly increasing as is the functional prognosis after surviving an OHCA. [1] This thesis contributes to the knowledge of rehabilitation treatment after an OHCA, to ensure that all patients who survive get the treatment they need at the right time and the right place. This thesis shows high survival rates of 43% in ambulance service treated OHCA in an optimised chain of survival (chapter 2). However, 23% of the patients referred for cardiac rehabilitation suffer from cognitive complaints (chapter 3). Those patients with cognitive complaints seem to have lower exercise capacity (chapter 4). This stresses the need for an integrated care pathway, that covers both neurological and cardiological aspects (chapter 5). Unfortunately, this type of care is not yet implemented throughout the Netherlands (chapter 6). Internationally, the need for integrated rehabilitation after OHCA is a focus point. This thesis describes most recent developments in this field (chapter 7).

The acute event

Out-of-hospital cardiac arrest

To optimise rehabilitation programs it is important to have an adequate picture of the population surviving an OHCA.
This thesis showed that survival rates of patients treated by an emergency medical service in the region Leiden, the Netherlands, are high: 42%. During the study period, all patients with an OHCA in our region were transported to a university medical center (the Leiden University Medical Center, LUMC), with transport mainly being carried out by one regional ambulance service ("Hollands Midden"). Earlier studies have shown that response times and the quality of hospital services are of major importance in improving survival rates after an OHCA.[2,3] The relatively high percentage of shockable rhythms found in our study (61%) indicates that arrival times of the ambulance service indeed where relatively short. One might therefore postulate that the efforts of further shortening arrival times by trained first responders (ambulance service or trained lay persons) and the concentration of acute treatment after OHCA to a specific hospital has contributed to these high survival rates.

It might be of interest to further study this hypothesis also in the light of the current efforts to increase the number of automatic external defibrillators (AEDs) and trained lay persons in the Netherlands.[4] Indeed, the high population density of the region Leiden may have contributed to the high survival rates. Many OHCA in our study were witnessed by bystanders (51%). Bystanders are able to call for help, thereby shortening the time between collapse and first responder. Subsequently they are able to start Cardio Pulmonary Resuscitation (CPR) almost immediately after the collapse, if necessary under supervision by high-quality Telephone-CPR of the dispatcher. The rapid use of AEDs, which are quite widely distributed in the Netherlands and available to all first responders, further increases the chance of obtaining return of spontaneous circulation.[5,6,7] An earlier study found that regions with high percentages of people that are able to provide BLS and sufficient AED's have better survival rates.[8] It would be interesting to know if there are major differences in The Netherlands in the number of people able to perform basic life support and the density of AED's employed.

New initiatives are undertaken to further improve the chain of survival, for example the creation of citizen responder networks.[6,9] Citizens who followed a CPR training are notified of a nearby cardiac arrest via SMS. The notified citizen can respond if he or she is able to assist. Instructions are given of the exact location where the person with the OHCA is or where the nearest AED is located. This way the arrival time of trained persons who can provide CPR and the quick arrival of an AED can be optimised. These developments need closely monitoring, as not only survival rates, but also sequelae might change.

Rehabilitation phase

After hospitalisation and surviving an OHCA with a cardiac cause, patients discharged home are eligible for a cardiac rehabilitation program.[7] With an increase of survivors after an OHCA, a parallel rise of the number of patients eligible for cardiac rehabilitation is expected.[7]

Screening for cognitive problems

Nearly all patients discharged home are classified by the hospital as having a good outcome, with a Cerebral Performance Category score of 1 or 2.[10] However, the mild cognitive aspects after an OHCA are not taken into account with this scoring system and are thus often overlooked. This is unfavourable, as mild cognitive deficits are known to negatively influence the quality of life of patients and their families or informal caregiver(s).[11,12]

As no generally accepted set of screening tools for mild cognitive problems after an OHCA was available, a short screening procedure comprising of the Mini-Mental State Examination (MMSE), Cognitive Failures Questionnaire (CFQ) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) was implemented in patients referred to cardiac rehabilitation. Using this set of screening tools, it was found that almost a quarter of the OHCA survivors attending a regular cardiac rehabilitation program experienced mild cognitive problems. This is less than the up to 42% that was observed in literature. One of the possible explanations for this discrepancy might lay in the properties of the MMSE. Since 2015, the resuscitation guidelines advise the Montreal Cognitive Assessment (MoCA) as a short cognitive screening instrument.[13] The MoCA, not widely available at the time we started our study, seems to be more sensitive to detect mild cognitive impairments than the MMSE.[14]

Remarkably, we found that the overlap of the MMSE, CFQ and to a lesser extent the IQCODE regarding the identification of possible cognitive problems was limited. This finding underlines that each of these instruments addresses different aspects of cognitive functioning. The CFQ, which was found to be complementary to the MMSE, seems to identify worries for cognitive slips instead of cognitive impairments, whereas the IQCODE is able to identify patients with an anosognosia. Our study showed that the IQCODE did indeed not identify the same patients as the MMSE. The lack of correlation could probably also be related to the timing of the administration of the IQCODE, approximately one month after the OHCA. This moment might be to early for the spouse to recognise cognitive problems. A study by Blennow Nordström in 2017 showed that when the questionnaire is assessed later, 6 months post cardiac arrest, it identifies a large number of patients with possible cognitive problems.[15] It would be interesting to perform more studies on this topic, as taking a questionnaire is more simple to implement than taking objective tests such as the MoCA.

Some patients who passed the cognitive screening without problems reported in our focus groups a comforting reassurance that their mental abilities seem to be unaffected (unpublished data). It would be interesting to study this topic, and also if they feel a post traumatic growth.[12]

Up till now, it is not known which screening test is best for OHCA-patients and international consensus is lacking. This hampers comparison of studies and populations. International effort on this point is desired. A thorough comparison between several screening tools and extensive neuropsychological testing should be performed in order to find a sensitive but concise screening after OHCA. In addition, further research is needed for the best moment to screen. In our study, patients were screened approximately one month after the OHCA. But one might also argue for an earlier (more sensitive) or later moment, when patients come out the initial euphoria of having survived and encounter the consequences of cognitive problems. We argue for a first screening relatively short after the OHCA in order to detect most prominent cognitive deficits. A follow up on a later moment is advisable to catch patients that encounter cognitive problems when cognitive needs increase. So far, also no studies have been performed on long term unmet needs.

An aspect that should be taken into account apart from cognitive functioning is emotional functioning. Anxiety and depression are

known to influence the mental state of the patient after an OHCA. [16,17] In conclusion, it is important to recognise and treat emotional problems after an OHCA not only because they may constitute an underlying reason for the diminished subjective cognitive functioning, but also for their known impact on new cardiac events and even on mortality.[18,19]

Cognition and physical exercise capacity

In literature there is convincing evidence that physical exercise has a positive effect on cognition.[20] Hardly any literature is available about the relation between cognitive impairments and exercise capacity. [21,22] This thesis suggests that patients with cognitive problems have a lower exercise capacity than patients without cognitive problems after an OHCA. From our small-sized study we can not draw any conclusions on causality, but one of the possible explanations might be that patients with a lower exercise capacity and cognitive impairments after an OHCA suffer from a more severe cardio vascular disease.[23] This theory is supported by the higher observed proportion of patients with diabetes in the cognitively impaired subgroup. Patients with diabetes have an increased risk of both cardiovascular diseases and also of cognitive deficits due to vascular cognitive impairments. However, the association could also be caused by the OHCA and its sequela itself. In that case one would expect a relationship between time of the arrest until ROSC, cardiac exercise capacity and cognitive impairments. Or, if there is a relation between size of the myocardial infarction and the brain damage, between troponin area under the curve and cognitive impairments. It might be worthwhile studying these issues, as more knowledge might make it easier to recognise the patients who are at risk for post anoxic encephalopathy.

A rehabilitation care pathway and its implementation

The Leiden care pathway was developed with the help of many patients. In several patient groups we discussed the logistics of the care pathway. A number of patients said that they were happy with the early screening for cognitive problems. The explanation of possible consequences took away their unmet need for information. At first we provided patients with a care pathway in which cardiac and cognitive rehabilitation were started simultaneously. However patients pointed out that this was to burdensome. They suggested to start with cardiac rehabilitation and

subsequently cognitive rehabilitation. A positive concomitant result of this choice was that neurologic symptoms, if present, had more time to dissolve spontaneously. It would be interesting to study if these choices are uniform across different countries and to compare the pathway with other treatment strategies.
The rehabilitation constructs in our care pathway were based on evidence from the literature on rehabilitation of patients after OHCA or other patient groups. Cognitive rehabilitation therapy addresses the interaction of cognitive, emotional and behavioural consequences of brain injury and teaches patients to use compensation strategies that cover their problems.[24,25] This approach is effective in other types of brain injury, but no proof is available for patients with post anoxic encephalopathy that suffer from both cognitive and cardiac impairments.[26] The same applies for cardiac rehabilitation strategies. Their efficacy is merely based on rehabilitation programs for patients after myocardial infarction or intra cardiac device placement. Cardiac rehabilitation seems to be safe for OHCA-patients though, but whether results are comparable is unknown.

Implementation of the guidelines
This thesis shows that guidelines on rehabilitation after OHCA are not widely implemented in The Netherlands.[13] Cognitive screening is not done routinely and objective tests are used even less. Formal integration of neurologic and cardiac rehabilitation are scarce. Besides, one of the studies in this thesis shows that knowledge on cognitive impairments is often insufficient in cardiac rehabilitation teams. On the other hand, many cognitive rehabilitation teams have limited knowledge on how to deal with physical limitations due to cardiac problems. For OHCA-patients with cognitive deficits both physical exercise training and cognitive rehabilitation treatment are important parts of their rehabilitation. If more evidence is available, quality of care might improve. Guidelines can describe the minimal requirements for the rehabilitation treatment of OHCA patients and the required skills and knowledge of care providers.
In order to study optimal rehabilitation strategies and to compare treatment protocols, international consensus on a concise set of outcome measures that covers most affected domains of skills and participation after OHCA is needed. Recently the Core Outcome Set for Cardiac Arrest initiative developed a core outcome set for cardiac arrest.[27] The core outcome set covers survival, neurological function,

and health-related quality of life at hospital discharge and at 30 days. Unfortunately, this core outcome set is not yet covering patient reported outcome measures on participation in the longer term.

Additional areas to be addressed in research in patients after OHCA

Besides all the above described subjects there are also important aspects which were not covered in our studies. In the following part we like to discus some of these areas.

The spouse, family and caregiver

During focus group meetings to evaluate our care path we realised how large the impact of the OHCA is on spouses, family and informal caretakers. The resuscitation, in some cases performed by themselves, the fact that their family member almost died and having seen someone seriously critical ill on the ICU should not be underestimated.[12] Spouses and other informal caregivers often show symptoms of anxiety, depression and even posttraumatic stress due to the serious event of an OHCA.[28,29] They are in need of information and emotional support. In our focus groups, some of the spouses had visited the hospital for cardiac complaints themselves. And almost all caregivers told us how difficult it was to leave the patient alone, even for a short while. This fear restricts the patient in his rehabilitation process and hampers the patient returning to his old lifestyle.

Currently, several best practices in care for patients after OHCA or other acute critically ill patients are available that involve caregivers. In the acute phase, the intensive care unit diaries developed by Christina Jones and her team seem to comfort spouses and fills in the gap in the patients memory, providing information that some patients are looking for.[30] In the Netherlands a structured educational program for patients and spouses delivered by a specialised nurse is available for the subacute phase.[29] This education program: "Stand still and move on" of Véronique Moulaert was found to lead to an improved quality of life, a better overall emotional state and less anxiety by the patients as compared to those who did not attend this education program. Another example is the internet project of Thomas Keeble at Basildon University Hospital, comprising peer support in a semi-open internet community for CA-survivors, which was appreciated by its users.[31]

Unfortunately, this community is only open to residents of the United Kingdom. In addition, in some countries resuscitation courses for spouses are given in order to decrease their stress levels.[32] It would be interesting to discuss with caregivers which interventions they feel are needed most. Also, the effect of integrated rehabilitation treatment on the caregivers burden has not been studied yet.
In the late phase, especially for spouses of patients with severe behavioural problems due to brain damage, cognitive behavioural group programs like PPEP4ALL are available.[33] The PPEP4ALL program has proven to be effective in patients with Parkinson's disease and pituitary disease. Based on our focus group observations at the start of this study, we planned a PPEP-study for our spouses. However, the integrated care pathway, which became operational before starting PPEP4ALL, resulted in not being able to find any spouses in need of such an additional intervention. So maybe we have solved their problems along the way in our integrated care pathway The PPEP4ALL program might be suitable though for OHCA survivors who are not eligible for attending the care pathway or do not want to attend a rehabilitation program.

OHCA of non-cardiac origin

Finally, we observed a lack of literature on cardiac arrest of non-cardiac origin (e.g. lack of oxygen, electrical shock, drugs abuse, severe haemorrhage) and possible cognitive sequalae. These patients may also experience cognitive and emotional problems that are similar or worse to that of patients after an OHCA of cardiac origin.[34,35] However, they are not routinely referred to cardiac rehabilitation and no other standardised care or screening is available for this group.

Conclusion

To conclude, this thesis has given insight into the patient group that survived an OHCA and gives directions to the development, evaluation and implementation of integrated rehabilitation treatment programs, with the ultimate goal being that all survivors and their spouses regain optimal quality of life and autonomy. Our studies showeded survivors of an OHCA attending a rehabilitation program may experience cognitive problems. A first attempt of identifying cognitive problems with a set of cognitive screening instruments in patients who attend a (cardiac)

rehabilitation program appeared to be feasible, although the screening needs further refinement. The finding that cognitive impairments have a negative effect on exercise capacity is important to take into account while further optimising the best rehabilitation program.Finally, the rehabilitation program should not only focus on the patient but also on the spouse or caregiver. By developing a core outcome set for rehabilitation the effectiveness of cognitive rehabilitation in OHCA patients and their relatives can be better evaluated.

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Chapter 9

Nederlandse samenvatting en Discussie

Nederlandse samenvatting en Discussie

In Nederland overleven jaarlijks ongeveer 3000 tot 3500 mensen een hartstilstand buiten het ziekenhuis door het snel en adequaat optreden van omstanders en ambulancedienst, de toename van beschikbare automatische externe defibrillators (AED's) en de goede zorg in ziekenhuizen. Na een succesvolle reanimatie en het ontslag uit het ziekenhuis breekt een periode van verwerking en herstel aan. Een revalidatietraject kan de patiënt en zijn of haar eventuele partner hierbij ondersteunen. Dit proefschrift beschrijft hoe de revalidatie voor mensen die een hartstilstand buiten het ziekenhuis hebben overleefd geoptimaliseerd kan worden. Extra aandacht gaat uit naar het cognitief functioneren na een hartstilstand. Cognitief functioneren omvat alle hersenprocessen die betrokken zijn bij het nadenken, zoals geheugen, planning en aandacht.

De introductie, hoofdstuk 1, beschrijft de definitie van een reanimatie en het percentage patiënten dat een hartstilstand overleeft door een succesvolle reanimatie. Tevens wordt een globale beschrijving gegeven van de geschiedenis van de reanimatie. Al sinds de oudheid wordt de mens geïntrigeerd door de 'plotse' dood. De reanimatie zoals wij die kennen, bestaande uit een combinatie van beademing en hartmassage, wordt sinds 1960 toegepast. Als er sprake is van een circulatiestilstand door een hartstilstand, geeft de toepassing van beademing en hartmassage de mogelijkheid om de circulatie zo optimaal mogelijk te houden tot er een defibrillator en professionele hulp beschikbaar zijn. De toepassing van alle deelhandelingen na een hartstilstand wordt ook wel de zogenaamde 'keten van overleving' genoemd. Deze keten van overleving is een model dat de verschillende stappen beschrijft die nodig zijn om de kans op overleving na een hartstilstand buiten het ziekenhuis te optimaliseren. Ongeveer 40% van de patiënten die buiten het ziekenhuis zijn gereanimeerd en dit overleven worden op korte en/of langere termijn geconfronteerd met de consequenties van zuurstoftekort in de hersenen (hypoxische ischemie). Het zuurstofgebrek kan leiden tot een lichte of ernstigere hersenbeschadiging, met als gevolg cognitieve problemen. Hoofdstuk 1 geeft een overzicht van de cognitieve problemen, die grote invloed kunnen hebben op het leven van patiënten.
Hoofdstuk 2 beschrijft een retrospectief onderzoek naar de overleving na reanimatie buiten het ziekenhuis in de regio Leiden. Deze regio heeft een goede zorgketen bestaande uit de ambulancevoorziening, politie en

brandweer, en één ziekenhuis waar alle patiënten worden opgevangen. De studie beschrijft, op basis van gegevens uit medische dossiers, de uitkomsten bij 242 patiënten die behandeld zijn door de Regionale Ambulance Voorziening Hollands Midden in de periode van april 2011 tot december 2012. Bij 76% (n=183) van de behandelde patiënten werd de circulatiestilstand veroorzaakt door een hartprobleem. Bij 67% (n=159) van de mensen met een circulatiestilstand was een getuige aanwezig en 51% (n=123) van de patiënten werden vóór de komst van politie, brandweer of ambulance al gereanimeerd door een getuige. Bij 39% (n=94) werd voor de komst van de ambulance een AED gebruikt tijdens de reanimatie. Van de 242 mensen overleden 74 patiënten (31%) op de spoedeisende hulp. Van de overige 168 patiënten vond bij 144 (60%) mensen een (sub) acute interventie plaats. Uiteindelijk werden 105 patiënten (43%) levend uit het ziekenhuis ontslagen. Factoren die een gunstige invloed op de overleving tot ontslag uit het ziekenhuis hadden waren: jongere leeftijd, een hartstilstand in de openbare ruimte, aanwezigheid van een getuige bij de hartstilstand, cardiale oorzaak met een hartritme dat met een AED behandeld kan worden, inzet van een AED, korte tijd van hartstilstand tot herstel van spontaan hartritme en betere bewustzijnstoestand tijdens vervoer in de ambulance. Deze studie toont een overleving van 43% in de regio Leiden van patiënten met een circulatiestilstand die behandeld zijn door de ambulancevoorziening en vervolgens opgevangen zijn op de spoedeisende hulp. Het lijkt waarschijnlijk dat dit relatief hoge percentage mede wordt gerealiseerd door de goede wijze waarop de keten van overleving tot uitvoer is gebracht.

In Nederland komen patiënten na een geslaagde reanimatie in aanmerking voor hartrevalidatie. Als leidraad voor de hartrevalidatie wordt de Nederlandse Multidisciplinaire Richtlijn Hartrevalidatie gevolgd. Een traject bij de hartrevalidatie duurt gemiddeld 12 weken en bestaat uit fysieke trainingen met daarnaast psychosociale begeleiding. Een deel van de patiënten die na een geslaagde reanimatie in aanmerking komen voor hartrevalidatie ervaart cognitieve problemen. Hoofdstuk 3 beschrijft een prospectieve cohortstudie die tot doel had om het cognitief functioneren in kaart te brengen van patiënten die deelnamen aan een hartrevalidatietraject. Aan deze studie namen 77 patiënten deel die tussen februari 2011 en februari 2013 werden verwezen voor hartrevalidatietraject bij het Rijnlands Revalidatie Centrum in Leiden. Alle patiënten ondergingen bij opname een screening met betrekking

tot het cognitief functioneren, bestaande uit de Mini-Mental State Exam (MMSE) en de Cognitive Failures Questionnaire (CFQ). Daarnaast werd de partner gevraagd de Informant Questionnaire on Cognitive Decline of the Elderly (IQCODE) in te vullen. Participatie en kwaliteit van leven werden gemeten met respectievelijk de vragenlijsten Impact op Participatie en Autonomie (IPA) en de Short Form SF-36 Health Survey.

Uit de screening bleek dat 28 (23%) van de geïncludeerde patiënten cognitieve problemen ervaarden. Achttien patiënten hadden een MMSE score lager dan 28, 10 patiënten hadden op de CFQ een score hoger dan 32 en 4 patiënten scoorden op de IQCODE hoger dan 3.6. Patiënten met cognitieve klachten hadden een lagere participatiescore en kwaliteit van leven dan patiënten zonder aanwijzingen voor cognitieve problemen.

De negatieve associatie tussen de aanwezigheid en mate van cognitieve problemen en kwaliteit van leven en participatie is al eerder, en ook bij andere aandoeningen aangetoond. Er is echter bij patiënten die een reanimatie buiten het ziekenhuis hebben overleefd weinig bekend over de relatie tussen cognitieve problemen en de fysieke gezondheid. Hoofdstuk 4 beschrijft een studie naar de inspanningscapaciteit van overlevenden van een circulatiestilstand buiten het ziekenhuis in relatie tot cognitieve klachten. Het onderzoek maakte gebruik van hetzelfde prospectieve cohort dat werd beschreven in hoofdstuk 3. Alle patiënten die na een succesvolle reanimatie worden verwezen naar de revalidatie ondergaan bij opname een inspanningsfietstest. Het doel van de studie was het vergelijken van de inspanningscapaciteit van patiënten met en zonder cognitieve problemen. Om voor het vergelijken tot homogene groepen te komen werden alleen patiënten geïncludeerd met een myocard infarct als oorzaak van de circulatiestilstand. Van 53 patiënten die aan dit criterium voldeden waren alle data van de inspanningstesten aanwezig. Negen van deze patiënten (17%) hadden cognitieve problemen volgens de MMSE, CFQ of de IQCODE. Er werden tussen patiënten met en zonder cognitieve problemen statistisch significante verschillen gevonden met betrekking tot zuurstofopname (VO2peak mediaan 14.5 vs. 19.7 ml/kg/min) en maximale cardiale belastbaarheid (mediaan 130.0 vs. 143.5 Watt; Metabole Equivalent of Tasks (MET) mediaan 4.1 vs. 5.6). Er werden geen verschillen gevonden in hartslag, systolische en diastolische bloeddruk tijdens rust en bij maximale inspanning. Ondanks dat dit een kleine studie was, werd

geconcludeerd dat er sprake is van een verband tussen cognitieve problemen en inspanningscapaciteit bij patiënten in revalidatie na een succesvolle reanimatie.

Vanwege de aanzienlijke kans op cognitieve problemen na een circulatiestilstand lijkt het wenselijk om tijdens de revalidatie bij alle patiënten aandacht te hebben voor mogelijke cognitieve problemen. Om de aandacht voor cognitieve problemen in te bedden beschrijft hoofdstuk 5 de opzet van een geïntegreerd zorgpad voor de revalidatiebehandeling na een succesvolle reanimatie. Het uiteindelijke doel van het revalidatiezorgpad is om de maatschappelijke participatie te bevorderen. Hoofdstuk 5 biedt handreikingen hoe de zorg kan worden afgestemd op de problemen en beperkingen van de individuele patiënt (fysiek, mentaal en cognitief) waarbij binnen het zorgpad duidelijke afspraken zijn gemaakt wie wat wanneer aanbiedt binnen het revalidatietraject van de patiënt. Het zorgpad werd ontwikkeld op basis van het best beschikbare bewijs (literatuuronderzoek) en expert opinion bestaande uit artsen, therapeuten, patiënten en hun eventuele partners.

Het zorgpad start na reanimatie in het ziekenhuis, bij de verwijzing naar een revalidatieprogramma. Alle patiënten die een circulatiestilstand hebben gehad op basis van een hartprobleem worden gescreend op cognitieve en emotionele problemen bij aanvang van de revalidatie met een makkelijk af te nemen en objectieve cognitieve screening. De cognitieve screening wordt aangevuld met vragenlijsten over ervaren cognitieve klachten door patiënt en partner. De hartrevalidatie bevat naast het fysieke en psychosociale programma voorlichting voor de patiënt en partner. Deze informatie gaat niet alleen over de fysieke gevolgen maar ook over de mogelijke cognitieve en emotionele gevolgen na een circulatiestilstand. Er is daarbij ook aandacht voor de partner, omdat bekend is dat de partner een grote kans heeft op post-traumatische stress, angst en depressie. De emoties van de partner belemmeren niet alleen de partner zelf, maar hebben ook een negatieve invloed op het herstel van de patiënt en zijn of haar deelname aan de maatschappij. Indien een patiënt lichte cognitieve klachten ervaart vindt de fysieke training plaats in kleine groepen zodat de patiënt begeleid wordt op zijn of haar eigen niveau. Na het volgen van 12 weken hartrevalidatie worden patiënten, indien nodig, verwezen voor een cognitief revalidatietraject. Tijdens de cognitieve

revalidatiebehandeling krijgen patiënt en partner uitleg over de cognitieve problemen, handvatten hoe om te gaan met de cognitieve problemen en wordt geoefend met compensatiestrategieën. Door de individuele benadering van de cognitieve revalidatiebehandeling is de duur van dit traject variabel.

Er zijn zowel Europese als Nederlandse richtlijnen voor de zorg van patiënten na een circulatiestilstand. Hoofdstuk 6 beschrijft een cross-sectionele studie waarin werd onderzocht in welke mate de aanbevelingen uit literatuur en richtlijnen worden opgevolgd binnen Nederland. De nadruk lag daarbij op het screenen voor cognitieve problemen na een reanimatie en het doorverwijzen naar cognitieve revalidatie. De vragenlijst is verstuurd naar medisch specialisten betrokken bij de revalidatie van gereanimeerde patiënten in Nederland. Het betrof 74 cardiologen van de Nederlandse Vereniging voor Cardiologie en het Landelijk Multidisciplinair Overleg Hartrevalidatie en 143 revalidatieartsen werkzaam binnen een instelling die lid is van Revalidatie Nederland of van de Werkgroep CVA Nederland. De digitale vragenlijst bevatte de volgende onderwerpen: kenmerken van de respondenten, gebruik en inhoud van cognitieve screening, inhoud van de revalidatie, organisatie van de zorg, behoefte aan een geïntegreerd zorgpad met zowel hartrevalidatie als cognitieve revalidatie, en belemmeringen en kansen voor een geïntegreerd zorgpad. Uiteindelijk werden vijfenveertig vragenlijsten retour ontvangen (van 16 cardiologen en 29 revalidatieartsen). Een meerderheid van de respondenten (n=39; 89%) onderschrijft de meerwaarde van een cognitieve screening binnen een geïntegreerd zorgpad voor patiënten na een succesvolle reanimatie. Zeventien (39%) respondenten gaven aan dat zij een vorm van cognitieve screening aanboden, waarbij 25% (n=11) gebruik maakte van een objectief meetinstrument. Belemmeringen voor de implementatie van een geïntegreerd zorgpad waren: onvoldoende kennis, logistieke problemen en een suboptimale samenwerking tussen medisch specialisten (cardiologen en revalidatieartsen). Deze studie laat zien dat een minderheid van de cardiologen en revalidatieartsen in Nederland standaard gebruik maakt van een cognitieve screening bij overlevenden van een circulatiestilstand. Het toepassen van een geïntegreerd zorgpad wordt gehinderd door gebrekkige kennis en organisatorische beperkingen. De lage respons op de verstuurde vragenlijst kan veroorzaakt zijn doordat meerdere artsen die betrokken waren bij de zorg van overlevenden van een circulatiestilstand van

eenzelfde locatie benaderd zijn. Over het algemeen bleek namelijk dat maximaal één specialist per locatie reageerde.

Hoofdstuk 7 geeft door middel van een narratieve review een overzicht van de meest recente literatuur over de revalidatiebehandeling voor overlevenden na een circulatiestilstand. Internationaal blijkt er overeenstemming dat overlevenden na een circulatiestilstand een geïntegreerd zorgpad aangeboden moeten krijgen, waarbij zowel cardiale als neurologische revalidatie aan bod komen. Tot op heden is nog weinig literatuur beschikbaar ten aanzien van de precieze invulling van revalidatie bij overlevenden na een circulatiestilstand. Vanuit de beschikbare onderzoeken lijkt het erop dat hartrevalidatie na een circulatiestilstand even effectief en veilig is als na een hartinfarct zonder circulatiestilstand. Om te screenen op cognitieve problemen en emotionele problemen na een circulatiestilstand lijken de objectieve Montreal Cognitive Assessment (MoCA) en de Hospital Anxiety en Depression Score (HADS) op dit moment het meest geschikt. Dit proefschrift toonde aan dat er aanwijzingen zijn dat patiënten met cognitieve problemen vermoedelijk een lager inspanningsniveau hebben. Het is verstandig hun revalidatieprogramma aan te passen aan zowel hun cognitieve als hun cardiale en fysieke mogelijkheden. Uit literatuur blijkt dat patiënten met ernstige cognitieve problemen gebaat zijn bij een individuele revalidatiebehandeling. Tijdens cognitieve revalidatie leren patiënten en hun omgeving compensatiestrategieën voor optimale participatie. Naast aandacht voor het fysieke en cognitieve deel heeft zowel de patiënt als de partner of mantelzorger baat bij emotionele ondersteuning. Er kan uiteindelijk geconcludeerd worden dat voor een optimale revalidatiebehandeling van overlevenden van een circulatiestilstand zowel expertise op cardiaal als cognitief gebied nodig is.

Discussie

De overleving en prognose na een circulatiestilstand verbeteren over de afgelopen decennia langzaam maar zeker.[1] Dit proefschrift beschrijft de huidige revalidatie voor patiënten na een circulatiestilstand en aanbevelingen voor optimalisering van de zorg.

De acute fase

Circulatiestilstand

In de regio Leiden is het overlevingspercentage van patiënten die behandeld zijn op de spoedeisende hulp na een circulatiestilstand 43%. Korte aanrijtijden en getuigen die snel starten met de reanimatie na de circulatiestilstand hebben een gunstig effect op de overleving.[2,3] Ook de beschikbaarheid van AED's in Nederland heeft een positief effect op de overleving.[5,6,7] Verder onderzoek naar de waargenomen verschillen binnen Nederland ten aanzien van beschikbare burgerhulpverleners en AED's is interessant.[4] In dit kader zijn nieuwe ontwikkelingen zich aan het richten op het optimaliseren van de keten van overleving, door het oprichten van netwerken met burgerhulpverleners die via een SMS worden gewaarschuwd om te komen reanimeren of een AED te brengen, zeer relevant.[6,8] Ook het effect van deze ontwikkeling moet verder onderzocht worden.

Revalidatie fase

Na het overleven van een circulatiestilstand met een cardiale oorzaak komt een patiënt in aanmerking voor hartrevalidatie.[7] Door de toename van overleving is een toename in patiënten te verwachten.

Screening op cognitieve problemen

Milde cognitieve problemen na een circulatiestilstand worden vaak niet herkend tijdens de ziekenhuisfase. Cognitieve problemen kunnen echter een grote invloed hebben op de kwaliteit van leven.[9,10] Door het ontbreken van consensus met betrekking tot de gewenste screening op cognitieve problemen na een circulatiestilstand werd ten behoeve van de studies in dit proefschrift een korte screenings-set samengesteld, bestaande uit de Mini-Mental State Examination (MMSE), Cognitive Failures Questionnaire (CFQ) en de Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Deze screening toonde aan dat bijna een kwart van de patiënten cognitieve klachten ervaart. Dit is minder hoog dan de percentages die genoemd worden in de literatuur (42%-50%). De oorzaak hiervan kan zijn dat de MMSE niet sensitief genoeg is.[12] Sinds 2015 wordt de recent ontwikkelde en sensitievere Montreal Cognitive Assessment (MoCA) geadviseerd als cognitieve screening.[11] Mogelijk speelt selectiebias ook een rol bij het verwijzen naar hartrevalidatie, waarbij een deel van de patiënten met cognitieve klachten niet wordt verwezen.

De overlap tussen de MMSE, CFQ en in mindere mate de IQCODE was beperkt. De CFQ en de IQCODE lijken verschillende aspecten van het cognitief functioneren te meten. De CFQ registreert eerder de zorgen omtrent cognitieve fouten dan cognitieve problemen. Ook de IQCODE, die bij de partner werd afgenomen, identificeerde andere patiënten dan de MMSE. Mogelijk detecteert de IQCODE eerder de zorgen die de partner zich maakt dan de cognitieve problemen. Het relatief vroege moment van afname in relatie tot de reanimatie in onze studie kan er bovendien aan bijdragen dat de partner de cognitieve problemen nog niet herkent. Bij afname van de vragenlijst 6 maanden later wordt door Blennow Nordström namelijk wel een groter aantal patiënten met cognitieve problemen gevonden.[13] Tot op heden is er geen overeenstemming bereikt welke screening het best is om het cognitief functioneren in kaart te brengen na een circulatiestilstand. Meer onderzoek is gewenst naar de inhoud van de screening en de optimale timing van de afname.

Cognitie en fysieke inspanning

Fysieke inspanning heeft een positieve invloed op cognitie, maar in welke mate cognitie van invloed is op fysieke inspanning is niet duidelijk.[14,15] Dit proefschrift laat zien dat er een vermoeden is dat patiënten met cognitieve problemen een lagere inspanningscapaciteit hebben. Ernstigere cardiovasculaire problemen kunnen hiervan de oorzaak zijn. [16] Dit vermoeden wordt versterkt door het relatief hoge aantal patiënten met diabetes in de cognitief aangedane groep. Een andere verklaring kan de circulatiestilstand zelf zijn, met een effect van de hypoxie op zowel de hersens als andere weefsels. Ook zouden patiënten met cognitieve klachten een meer sedentaire levensstijl kunnen hebben. Het lijkt zinvol om hier meer onderzoek naar te doen zodat er beter rekening gehouden kan worden met beïnvloedbare factoren binnen het revalidatieprogramma.

Een revalidatiezorgpad en de implementatie

Het Leidse zorgpad werd ontwikkeld met hulp van patiënten en hun partners. In focusgroepen bespraken we de logistiek van het zorgpad. Patiënten gaven aan blij te zijn met de vroege cognitieve screening. Een positief effect van de screening is dat patiënten aangeven het fijn vinden om bevestigd te krijgen dat er op cognitief vlak geen problemen

lijken te zijn. (niet gepubliceerde data uit focusgroeponderzoek). Er treedt mogelijk zelfs zogenaamde posttraumatische groei op, waarbij mensen aangeven na de circulatiestilstand meer van het leven te gaan genieten en een betere kwaliteit van leven te krijgen. Deze gedachten over posttraumatische groei nodigen uit tot meer onderzoek. [10]

De evaluatie van het zorgpad bij patiënten door middel van focusgroep interviews maakte duidelijk dat de uitleg van mogelijke gevolgen tegemoet kwam aan hun behoefte aan informatie. Het gelijktijdig starten van de hartrevalidatie en cognitieve revalidatie werd als te belastend ervaren en patiënten stelden voor om te beginnen met de hartrevalidatie met vervolgens zo nodig cognitieve revalidatie. Een positief resultaat van deze verandering was dat neurologische symptomen, indien aanwezig, meer tijd hadden om spontaan te herstellen. Toekomstig onderzoek zou zich moeten richten of de keuzes van patiënten in dit opzicht uniform zijn in verschillende landen en om het huidige zorgpad te vergelijken met andere behandelingsstrategieën.

Cognitieve revalidatie benadert de gevolgen van hersenletsel op het vlak van cognitie, emotie en gedrag en leert patiënten compensatiestrategieën te gebruiken.[17,18] Deze aanpak is effectief bij andere doelgroepen met hersenletsel, er is echter geen bewijs beschikbaar voor patiënten met post-anoxische encefalopathie die beperkingen hebben op cognitief als cardiaal gebied.[19] Hetzelfde geldt voor het effect van hartrevalidatie. Hartrevalidatie lijkt veilig voor patiënten na een circulatiestoornis, maar de kennis over het effect is gebaseerd op revalidatieprogramma's voor patiënten na een myocardinfarct of een intra-cardiale interventie zonder hartstilstand. Of resultaten vergelijkbaar zijn moet verder onderzocht worden.

Implementatie van de richtlijnen

De resultaten van de enquête over de zorg na reanimatie tijdens de revalidatie onder revalidatieartsen en cardiologen maken duidelijk dat er in Nederland ruimte is voor verbetering van de implementatie van richtlijnen over revalidatie na een circulatiestilstand.[11] Een cognitieve screening wordt niet routinematig uitgevoerd, en objectieve tests worden nog minder gebruikt. Formele samenwerkingen tussen cognitieve- en hartrevalidatie zijn schaars. Daarbij toont dit proefschrift aan dat kennis over cognitieve stoornissen vaak onvoldoende is bij

hartrevalidatieteams en dat cognitieve revalidatieteams beperkte kennis hebben over de fysieke belasting bij cardiale problemen. De fysieke trainingen en de cognitieve revalidatiebehandeling zijn beiden belangrijk binnen de revalidatie van patiënten na een circulatiestilstand. Meer onderzoek naar de inhoud van de behandeling verbetert de kwaliteit van de zorg. Om verder onderzoek te doen naar optimale revalidatiestrategieën en het vergelijken van behandelprotocollen is internationale overeenstemming nodig om tot een basisset van uitkomstmaten te komen die de meest aangedane domeinen bestrijkt. Recent is de Core Outcome Set for Cardiac Arrest ontwikkeld. Deze set bevat uitkomstmaten ten aanzien van overleving, neurologisch functioneren, en kwaliteit van leven gerelateerd aan gezondheid bij ontslag uit het ziekenhuid en na 30 dagen.[20] Helaas valt maatschappelijke participatie op de langere termijn (werk, hobby's, sport en andere tijdsbesteding) niet onder deze basisset.

Overige aandachtspunten

Naast bovengenoemde onderwerpen zijn er nog een aantal aspecten die niet direct bestudeerd zijn in het kader van dit promotieonderzoek, maar wel het noemen waard zijn.

De partner, familie of mantelzorger

Tijdens het evalueren van het zorgpad door middel van focusgroepen werd duidelijk hoe groot de impact van een circulatiestilstand is voor de partner, familie of mantelzorger. De impact van het feit dat hun familielid bijna overleden was en in kritieke toestand op de intensive care lag moet niet onderschat worden.[10] Vaak vertoont deze groep dan ook symptomen van angst, depressie of posttraumatische stress[21,22] en is er behoefte aan informatie en emotionele begeleiding. Een aantal methoden, gebaseerd op best practice, zijn beschikbaar om tegemoet te komen aan deze problemen. In de acute fase is het zogenaamde intensive care dagboek beschikbaar, ontwikkeld door Christina Jones. Dit dagboek geeft de betrokken familie en mantelzorger steun en kan op een later tijdstip de gaten in het geheugen van de patiënt opvullen. [23] Ook is er een educatief programma beschikbaar voor de patiënt en partner in de subacute fase.[22] Dit programma 'Stilstaan en doorgaan", ontwikkeld door Dr. Véronique Moulaert uit Nederland leidt tot een betere kwaliteit van leven, beter emotionele gesteldheid en minder angst [29]. Thomas Keeble, cardioloog, van Basildon University Hospital

in het Verenigd Koninkrijk startte een semi open internetgroep voor patiënten die een circulatiestilstand hadden overleefd.[24] In sommige landen is een reanimatiecursus beschikbaar voor partners om stress te verminderen.[25] Aan het eind van de revalidatie kan een cognitieve gedragsgroep zoals het Patiënt en Partner Educatie Programma voor Alle chronische ziekten (PPEP4ALL) van meerwaarde zijn.[26] PPEP4ALL is een zelfmanagement educatieprogramma voor mensen met een (chronische) ziekte en de partner of mantelzorger. Het programma heeft tot doel om de persoon met de aandoening als ook de partner handvatten te geven om met psychische en psychosociale gevolgen om te gaan. Het programma blijkt al effectief te zijn voor andere groepen patiënten met een combinatie van cognitieve en lichamelijke klachten, zoals de ziekte van Parkinson en hypofyseziekte. Voor de toekomst is het interessant om te kijken welke interventies het meest opleveren vanuit het oogpunt van de partner en mantelzorgers. Ook is het effect van het geïntegreerde zorgpad voor partners niet onderzocht.

Circulatiestilstand zonder cardiale oorzaak

Het voorkomen van cognitieve problemen bij mensen na een circulatiestoornis met een niet-cardiale oorzaak (bijv. verstikking, verdrinking, elektrocutie, drugsmisbruik, ernstige bloedverlies) is in de literatuur nauwelijks beschreven. Deze patiënten kunnen echter ook cognitieve en emotionele problemen ervaren die vergelijkbaar of zelfs ernstiger zijn dan de patiënten met een circulatiestilstand ten gevolge van een cardiale problematiek. [27,28] Deze groep patiënten wordt op dit moment in Nederland niet standaard verwezen naar (hart)revalidatie en er is geen gestandaardiseerde zorg of screening beschikbaar. Onderzoek naar en aandacht voor fysieke, emotionele en cognitieve problemen in deze groep patiënten lijkt gewenst.

Referenties

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Chapter 10

List of publications
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Dankwoord

List of publications

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Curriculum vitae

Liesbeth Wilkea van der Wal werd geboren in Wageningen op 31 maart 1974. In 1992 behaalde zij haar diploma aan het Hoger Algemeen Voortgezet Onderwijs (HAVO) aan het Wagenings Lyceum in Wageningen. Na een jaar Pedagogische Academie voor het Basisonderwijs (PABO) in Utrecht begon zij in 1993 aan de Opleiding Logopedie en Foniatrie aan de Hanzehogeschool Groningen. Na het behalen van haar diploma in 1997 startte zij aan de Rijksuniversiteit van Groningen met de opleiding Neurolinguïstiek, onderdeel van de studierichting Algemene Taalwetenschappen. In 1999 behaalde zij haar doctoraaldiploma Klinische Neurolinguïstiek.

In 2000 begon Liesbeth als logopedist in een vrijgevestigde logopedische praktijk om vervolgens in Amsterdam te gaan werken bij twee verpleeghuizen, De Poort en de Amstelhof, op somatische, psychogeriatrische en Korsakov afdelingen. In 2002 startte zij als logopedist bij het Zeehospitium te Katwijk en zij bleef daar werkzaam toen de organisatie na een verhuizing naar Leiden het Rijnlands Revalidatie Centrum (RRC) werd. Vanaf 2008 combineerde zij daar haar functie als logopedist met die van klinisch neurolinguïst.

In 2011 begon Liesbeth als projectmedewerker in het RRC-project 'zorgpad post-anoxische encefalopathie na reanimatie'. Het doel van dit project was het optimaliseren van de revalidatiebehandeling voor patiënten met een post-anoxische encefalopathie na reanimatie. In 2016 startte zij het promotieonderzoek beschreven in dit proefschrift onder leiding van Prof.Dr. Thea Vliet Vlieland en Dr. Paulien Goossens. De redactie van The Netherlands Heart Journal reikte haar in 2015 de Durrerprijs, uit voor het artikel beschreven in Hoofdstuk 2 van dit proefschrift. In 2017 ontving zij van de Hersenstichting de Hersenbokaal vanwege de actieve rol die zij speelt bij het vertalen van haar wetenschappelijke kennis en ervaring naar zowel het professionele als het lekenpubliek.

Naast bovenstaande werkzaamheden is Liesbeth altijd actief geweest in verschillende nevenactiviteiten. Zij was bestuurslid van de sectie gezondheidszorg van de Nederlandse Vereniging voor Logopedie en Foniatrie. Zij was gedurende twee perioden lid van de ondernemingsraad van het Rijnlands Revalidatie Centrum (sinds 2019 Basalt Revalidatie). Na een periode als oudervertegenwoordiger bij Scouting Sint Jozef Leiden, is zij momenteel algemeen bestuurslid van deze vereniging.

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