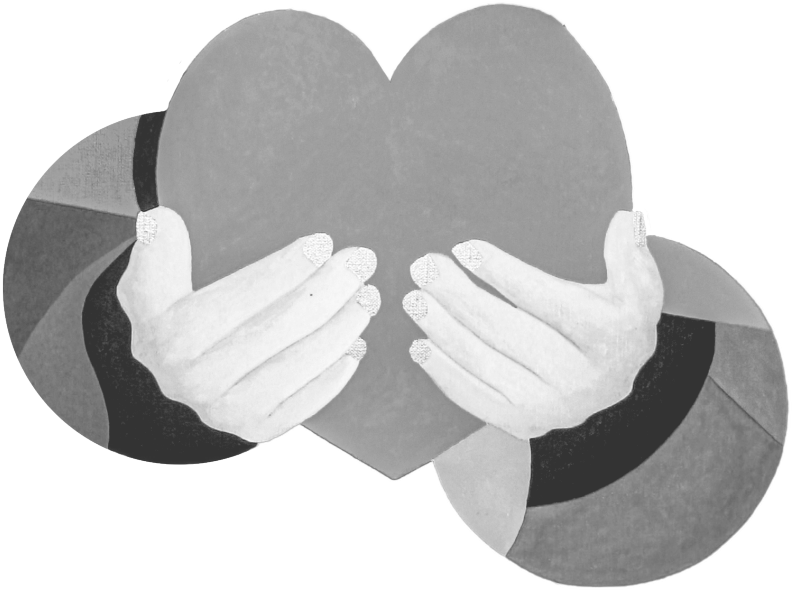
Rehabilitation after Resuscitation

Wal, L.W. van der

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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