Out-of-hospital circulatory arrest: factors determining the outcome Amsterdam resuscitation study (ARREST) 2 and 3
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Chapter 9
Out-of-hospital cardiopulmonary resuscitation:
The chain of quality of survival?

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Abstract

Care should be taken that harm (a remaining poor quality of life) after out-of-hospital cardiopulmonary resuscitation (OOH CPR) not outweighs the possible benefit of surviving. Prospective cohort study between June 1, 1995 and August 1, 1997 including patients identified through the database of the Amsterdam Resuscitation Study. We investigated the impact of the time-related dynamics of the chain of survival (OOH CPR) on the quality of life of survivors, taking also into account the patient characteristics. Quality of life was measured by means of the Sickness Impact Profile (SIP). Cognitive functioning was assessed in depth through the Mini Mental State Examination. SIP profiles were compared to profiles of other populations. From the 1285 included patients 150 (12%) survived to hospital discharge. A total of 112 were definitive survivors and available for further assessment. The SIP profile of survivors was just above the profile of the open Dutch population of elderly, indicating only a slightly poorer quality of life. Of the patients characteristics female gender and pre-arrest cardiac and noncardiac morbidity were significant associated with an impaired physical functioning (OR 3.8, 95%CI 1.2-12.3, OR 10.4, 95%CI 1.2-89.4 respectively). Of the links of the chain of survival, only the need for ALS was statistically associated with an impaired cognitive functioning (OR 0.2, 95%CI 0.05-0.6). Clinically important time trends were found suggesting better quality of life outcomes after early access, early basic life support, early defibrillation and early advanced life support. Functioning was not clearly linear associated with the delays in the chain of survival. Pre-arrest cardiac comorbidities in combination with noncardiac comorbidities determine health outcomes after CPR. This may have implications with regard to decision making about do not resuscitation policy. Although early interventions are associated with the best outcome, there is no evidence to support the opinion that, because of the fear of causing harm, CPR should be withheld to cardiac arrest patients who suffer from delayed response times.

1. Introduction

Cardiopulmonary resuscitation (CPR) is a last resort medical intervention when there seems little to loose and much to win. Still care should be taken that the risk of harm, related to CPR (a remaining poor quality of life), not outweighs the possible benefit of surviving. Eisenberg, referring to the medical principle “first do no harm”, recently even warned that modern technology and pharmacology can sometimes bring persons back to life with “hearts too bad to live”.1

The four links in the chain are well known contributors to survival: early access to the emergency medical system, early Basic Life Support (BLS), early defibrillation and early Advanced Life Support (ALS).2 Harm after out-of-hospital (OOH) CPR can be evaluated by associating the time related dynamics of the chain of survival with the quality of life of survivors. Not all of the delays in the links have proven to be related to poor neurological outcome. Conflicting evidence exists for delayed BLS,1,4 and delayed ALS3,5 supporting evidence is presented for delayed defibrillation.4,6,7 This evidence derives from a few studies, mainly focusing on a part of the chain or for a selected group of patients (only VF as initial rhythm). Furthermore, the studies concentrated only on neurologic outcome. Neurologic impairments are of course important, but not synonymous to quality of life. The latter has several other dimensions, such as a physical and psychosocial dimension, and these are preferably evaluated simultaneously.8 One should realize that poor quality of life after CPR can also be associated with patient characteristics such as age, gender and comorbidity before cardiac arrest.9 The purpose of this study is to investigate the harm after OOH CPR, and the extent to which the time related dynamics of OOH CPR are associated with the quality of life of the survivors, taking into account the patient characteristics.
2. Patients and methods

2.1. Study design

The study was carried out in Amsterdam and its surrounding areas. It's emergency medical service (EMS) system serves a population of 1.3 million inhabitants. The system consists of one central dispatch center and has one single tier: fully equipped ambulances, staffed with trained nurses and trained drivers. These crews perform ALS according to a national protocol based on international guidelines.\textsuperscript{10,11}

Patients were prospectively identified through the database of the Amsterdam Resuscitation Study.\textsuperscript{12} This registry collected all, by the ambulance personnel confirmed OOH cardiac arrests, between June 1, 1995 and August 1, 1997. During this period, research personnel alarmed by the dispatch center immediately attended each cardiac arrest. Data from the scene up to hospital admission were prospectively collected according the Utstein style.\textsuperscript{11} Included in this study were all consecutive survivors of OOH cardiac arrest (age ≥ 18 years) discharged alive from the hospital. Medical ethics committees of all participating institutes approved the study, patients and relatives gave an informed consent.

2.2. Outcome measures

Survivors were interviewed at home at least three months after their discharge, to allow for a sufficient period to recover. Quality of life was evaluated by physical, psychosocial functioning. Cognitive functioning was assessed in depth. The questionnaires were selected by their psychometric properties and were already used in other CPR studies.\textsuperscript{14-15} Quality of life was measured with the 136-item self-reporting Sickness Impact Profile (SIP) with 12 subscales and to aggregated subdimensions (physical and psychosocial health).\textsuperscript{17} SIP scores range from 0 to 100, higher scores indicate a worse quality of life. Patients were arbitrarily classified as physical and psychosocial impaired when they exceeded more than 1 Z-score from the sample mean (Z score = individual patient score - sample mean / SD sample mean).

Cognitive functioning was assessed with the 30-item Mini Mental State Examination (MMSE). Patients were classified as cognitive impaired at a cut-off score of ≤ 23.\textsuperscript{18} The level of dependence on others was assessed with the Rankin scale.\textsuperscript{19}

Following the Utstein recommendations, patients were classified according the Overall and Cerebral Performance Categories (OPC and CPC).\textsuperscript{20} In case of patients who could not respond to the SIP and MMSE questionnaires, because of, for example, poor cognitive functioning, we assessed the patients through interviews with their close relatives using a proxy-versions of the SIP. There is no proxy assessment for the MMSE and therefore the MMSE scores of these non-communicative patients were set to zero, expressing a worst case scenario.

2.3. Patient characteristics and definitions

Data of comorbidities were collected from the medical records of the hospital and the patients' general practitioner, who have a full record on the patients' medical history. Comorbidity was categorized into no comorbidity, cardiac, noncardiac or both using the International Classification of Diseases -9\textsuperscript{th} revision (ICD-9 codes). A shockable initial rhythm was ventricular fibrillation or ventricular tachycardia as the first recorded heart rhythm. The duration of the circulatory arrest was defined as the time interval from collapse to the definitive return of the spontaneous circulation (ROSC).

2.4. System characteristics and definitions

The data from the system characteristics were described according the chain of survival. The time intervals were calculated from collapse: (a) to the call to the dispatch center, (b) to BLS, (c) to the first defibrillation, (d) and to ALS (endotracheal intubation and/or intravenous medication).
When a patient collapsed after the call and in presence of the EMS personnel, this was coded as 'EMS witnessed. When ROSC and spontaneous ventilation occurred before ALS measures could be taken, this was defined as 'ALS not needed'.

2.5. Statistical analysis

To express the health state of the survivors after OOH CPR and possible harm related to CPR, we contrasted the SIP scores of our study group of survivors after OOH CPR with (1) a population with a known seriously impaired quality of life (stroke patients of about the same age),21 (2) with a general Dutch open population of elderly,22 and (3) with a population after in-hospital CPR, previously reported by our study group.9 The scores of the open population were set to zero (most favorable quality of life) using D-transformation (SIP mean score OOH CPR group minus SIP mean score open population / SIP score SD open population).

To express the impact of patient characteristics and time related dynamics of the chain of survival, we first entered dichotomous variables such gender, presence of the ambulance, EMS witness, shockable rhythm, and need for ALS in separate logistic regression models using impaired cognitive functioning [MMSE ≤ 23], physical and psychosocial functioning (SIP Z score ≥ 1) as dependent variables. Secondly, continuous time variables were made categorical (dummy coded) by arbitrarily dividing them into segments taking into account the distribution and medical relevance. We evaluated these in separate logistic regression models using the same dependent variables. Independent variables were the various time intervals and the age of the patients.

Thirdly, to estimate the independent effect of patient characteristics in conjunction with the time related dynamics of the chain of survival on impaired cognitive (MMSE) physical and psychosocial functioning (SIP) after survival, we used again multivariate logistic regression (backward elimination) with the MMSE and SIP physical and psychosocial scores as dependent variable. Because of anticipated small subgroups, we used liberal entry and removal criteria, p ≤ 0.20 and p ≥ 0.10 respectively. The effect sizes calculated by the logistic models were expressed as odds ratios (OR) and their 95% confidence intervals (CI). A p-value of less than 0.05 was considered statistically significant. Analyses were performed using SPSS 11 on Windows NT.

3. Results

3.1. Study population

During the study period 1285 patients underwent CPR, 369 patients initially survived to hospital admission, 150 (12%) survived to hospital discharge. Eleven/150 patients (7%) died after discharge and before the interview. Their median OPC score obtained at the moment of hospital discharge was two and the median CPC score was one. Seven/150 patients (5%) were < 18 years of age and excluded, while 10/150 (7%) were lost to follow-up. At follow-up 10/150 (7%) survivors refused to participate, five of these reported a good health, one a bad health and four would not answer any questions on their current health. Eventually, 112 survivors were interviewed for this study. The median time from the day of cardiac arrest to interview was 8 months (range: 4-20 months).
Figure 1. Sickness Impact profiles comparing patients after stroke, in-hospital CPR, and out-of-hospital CPR with a reference group of an open population of Dutch elderly (zero score).

3.2. Patient characteristics

Of the 112 survivors, 108 were Caucasian (97%), 93 were men (83%), and had a mean age of 61 (SD 13). Twenty seven percent had no previous comorbidity. Of those with comorbidity, the presence of only noncardiac comorbidity was the least frequent (13%). The median arrest duration (time from collapse to ROSC) was 10 minutes (ranging from 1 to 28 minutes).

3.3. Functional outcome

Eighty percent of the survivors were independent from the help of others (Ranking scale 1 and 2). An impaired physical functioning was found in 16/112 survivors (14%), 14 (13%) had an impaired psychosocial functioning and 19 (17%) had signs of an impaired cognitive functioning (MMSE score ≤ 23). Forty-seven percent (9/19) of these had also an impaired physical and psychosocial functioning.

Of the 112 survivors the median CPC score was one, eight (7%) had a CPC score of ≥ 3 indicating poor cerebral performance. The median OPC score was two, 13 (12%) had a score of ≥ 3 indicating poor overall performance.

3.4. Quality of Life of the survivors after OOH CPR compared to other patient populations

Comparing the quality of life profile of survivors after OOH cardiac arrest with other populations, the survivors profile was just above the open Dutch population of elderly (Figure 1). The D-scores ranged from 0.25 for body care and movement to 0.79 and 0.82 for total psychosocial functioning and total overall functioning, indicating a slightly poorer quality of life.

The quality of life profile of survivors after in-hospital cardiac arrest was above the profile of survivors after OOH cardiac arrest, indicating a slightly poorer quality of life. Compared to the
open Dutch population, scores of survivors after in-hospital cardiac arrest ranged from 0.66 for mobility to 1.41 for eating. Patients after stroke had the worst quality of life, with score differences from the open population ranging from 0.99 for social interaction to 2.8 for communication.

![Distribution of patients (n=112) and odds ratios for cognitive (MMSE), physical (SIP), and psychosocial (SIP) functioning.](image)

**Figure 2.** Patient characteristics of survivors related to cognitive (MMSE), physical and psychosocial (SIP) functioning (odds ratios and 95% confidence intervals). Ref is reference group.

### 3.5. Patient characteristics related to impaired cognitive functioning, physical and psychosocial functioning

Older age was not significantly associated with an impaired cognitive, physical and psychosocial functioning (Figure 2). Seventeen percent of the survivors were female, and female gender was significant associated with an impaired physical functioning (OR 3.8, 95%CI 1.2-12.3), but not with cognitive and psychosocial functioning. Twenty eight percent of the survivors had cardiac as well as noncardiac comorbidity and this was significantly associated with impaired physical functioning (OR 10.4, 95%CI 1.2-89.4), but not with cognitive and psychosocial functioning. The order of impact of comorbidity on impaired cognitive, physical and psychosocial functioning was similar, with the least impact for patients without comorbidity and the most impact on those with noncardiac and both a cardiac and noncardiac comorbidity.

### 3.6. Chain of survival related to impaired physical, psychosocial and cognitive functioning

Forty five percent of the calls to the dispatch center occurred before the collapse and concerned conscious patients with severe complaints or symptoms. In these cases the ambulance was already moving or present at onset of the cardiac arrest (Figure 3, left column). A trend could be observed pointing to a low OR for impaired cognitive, physical and psychological functioning when ambulance is moving or present and high ORs were found with an increasing delay in the call when the collapse already had occurred.

Thirty five percent of the survivors received BLS by the ambulance at onset of their cardiac arrest (Figure 3, left column, EMS witnessed). BLS by the EMS personnel tended to be associated with better cognitive and psychosocial functioning compared to BLS by bystanders, while and delayed BLS by bystanders (> 1 minute after onset of cardiac arrest) tended to be associated with an impaired cognitive and physical functioning, although this was not statistically significant.

Nine percent of our survivors did not require a defibrillatory shock. Delayed defibrillation (5 and more minutes after onset) tended to be associated with impaired cognitive functioning, but this was not statistically significant.
Fifty percent of the survivors did not need ALS. This was statistically associated with better cognitive functioning (OR 0.2, 95%CI 0.05-0.6), but not with a better physical and psychosocial functioning. A trend can be observed suggesting that delayed ALS is associated with impaired cognitive and particular impaired physical and psychosocial functioning.

3.7. Independent impact of patient and system characteristics on physical, psychosocial and cognitive functioning

Upon entering all patient characteristics and the characteristics of the chain of survival with a p-value < 0.20 into logistic regression models (backward elimination) with cognitive, physical and psychosocial functioning as dependent variable, all models showed effects of comorbit and the need for ALS on the various domains of quality of life.

Cognitive functioning was negatively influenced by pre-arrest noncardiac comorbidity and the combination of pre-arrest cardiac and noncardiac comorbidity (respectively OR 4.3, 95%CI 0.95-19.7; OR 3.5, 95%CI 1.1-17.8). Cognitive functioning was positively influenced by the absence for the need of ALS (OR 0.18, 95%CI 0.05-0.60). Physical functioning was only significantly negatively influenced by the combination of cardiac and noncardiac comorbidities (OR 9.1, 95%CI 1.1-79.0), and tended to be negatively influenced by noncardiac comorbidities (OR 7.7, 95%CI 0.7-83.3). Physical functioning tended to be positively influenced by the absence for the need of ALS (OR 0.38, 95%CI 0.11-1.2).

Psychosocial functioning tended to be negatively associated with the combination of cardiac and noncardiac comorbidities (OR 3.0, 95%CI 0.81-10.9) and BLS by the ambulance at the beginning of onset of the cardiac arrest (OR 0.25, 95%CI 0.05-1.3).

Sensitivity analysis with different cut-off values for good/poor cognitive, physical and psychological functioning did not yield statistically different results. In a subgroup analysis of patients with a shockable initial rhythm, we could not demonstrate that the time to defibrillation had a statistically independent effect on cognitive functioning.
4. Discussion

Our study demonstrates that the quality of survival after OOH CPR, relative to other patient populations, is acceptable and also acceptable when based upon absolute numbers, 80% of the survivors function independent from the help of others. There appears to be a relation between the time related dynamics of the chain of survival and the cognitive, physical and psychosocial functioning of the survivors, indicating that the earliest interventions are associated with best outcomes. Poor outcomes are best explained by complex pre-arrest morbidity and good outcomes by the absence of the need for ALS.

The positive health outcomes, compared to other studies could have resulted from a certain selection in our study by (a) survivors in a poor condition that died before the quality of life assessment, (b) through a selective loss to follow up, or (c) by a selective non-response. Indeed, the interval between cardiac arrest and the assessment (median 8 months) may result in the phenomenon of the “survival of the fittest”. However, of the survivors who where discharged but died before the assessment, we calculated OPC and CPC scores from the medical records at the moment of hospital discharge, and their cerebral and overall status was good (median CPC 1, OPC 2).

We choose not to assess the health outcomes earlier, since it is essential to allow patients to recover and we believe that this achieved health state is the most relevant for medical decision making. The most severely cerebral damaged patients were not analyzed in this study, since they died before hospital discharge. Of the survivors lost to follow-up (n = 10), we carried out a thorough search. We believe that they are alive and not living in a nursing home, because this requires a civil and insurance registration. Of the non-responders, we reported that at least half of this group is in good health, while non-communicative participating survivors were assessed through their proxies and their data are included in the study. All by all, there is no reason to believe that our study is biased towards too optimistic outcomes.

A limitation is the statistical power in the subgroups to establish time-related effects on an impaired functioning after an OOH cardiac arrest. Small groups of survivors are inherent to the outcome of CPR. Larger study cohorts can only assembled in a relatively short time frame by pooling data from other studies. Pooling data is difficult, and requires identical outcome measures across studies. There is no international excepted standard, except for the OPC and CPC measure. These scores are, however, more suitable for classifying patients than for measuring functional outcomes in a sensitive manner.

It is already known that the initiation of BLS and early defibrillation improve the neurological outcomes after CPR, our study is original in the fact that data are analyzed in great detail and that we exactly quantify the impact of all time related dynamics of the chain of survival on multiple domains of quality of life. Further more we uniquely demonstrate the impact of pre-arrest morbidity and the absence of the need for ALS on the outcomes.

There is a common clinical belief that long time delays in links of the chain of survival cause death, and if not, these delays at least induce a poor quality of life. This assumption is not supported by our study results. In the univariate analysis some trend suggest a linear relationship between the dynamics of the chain of survival and the neurological outcome (early access). Trends in BLS, defibrillation and ALS intervals point to a possible non-linear relation between the time interval and the neurological outcome, suggesting that (a) cerebral damage occurs soon after the cardiac arrest onset; (b) that extended intervals to call, BLS, and defibrillation not increase cerebral harm; and (c) that thus only extreme enhancements in the time related dynamics of the chain of survival may lead to improved health outcomes.
The absence of the need for ALS interventions (shorter CPR procedures) had a significant impact on better neurological outcome. In turn, the need for ALS does not imply a poor neurological outcome per se; four of the 19 patients who received delayed ALS were not neurologically impaired. We feel a medical dilemma and that is that the harm to benefit ratio when ALS is required is about 4:1. Since neurological impairment does not exclude a live appreciated by patients, we do not suggest to withhold ALS measures when indicated.

We specifically demonstrated the impact of pre-arrest morbidity; these results are in essence similar to our previous studies of the in-hospital cardiac arrest population. It seems that the fear of clinicians, that modern technology and pharmacology can sometimes bring persons back to life with “hearts too bad to live” specifically counts for patients who already had a poor condition before cardiac arrest. Particular those with cardiac, in combination of noncardiac comorbidities, like stroke, renal failure and diabetes mellitus are predictors for an impaired outcome. Since these factors are known before cardiac arrest, they can be used in physician initiated discussions about withholding CPR under some conditions.

In summary, patients after an out-of-hospital resuscitation are in a relatively good state of health. Complex pre-arrest morbidity has proven to be strongly related to impaired health outcomes and more strongly contribute to the outcomes than the links of the chain of survival. We feel there is some medical ground justification to decide to withhold CPR in the field based on the medical history of the patient, when taken into account his/hers preference for resuscitation. Such decision should most preferably be taken prior to arrest and not during ongoing resuscitation effort.

Although not statistically proven, we believe that impaired health outcomes can be occur after even moderate delays in the links of the chain of survival. We are convinced that only large improvements in the system related factors of the chain of survival might result in improved health outcomes after OOH resuscitation. Such improvements may be delivered by automated defibrillators for public access or in the homes of high-risk populations, because this greatly reduces delays in the chain of survival.

There is no evidence to support the general opinion that, because of the fear of causing harm, CPR should be withheld to cardiac arrest patients who suffer form delayed response times.

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References
