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Clinical paper

Alterations in cognitive outcome between 3 and 12 months in survivors of out-of-hospital cardiac arrest

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ABSTRACT

Objectives: To prospectively investigate cognitive recovery from 3 to 12 months after resuscitation from out-of-hospital cardiac arrest (OHCA) and the associations between cognitive performance at 3 months and health-related quality of life (HRQL), psychological distress and work status after 12 months.
Methods: At both assessments, neuropsychological tests were used to measure aspects of general mental ability, verbal and visual memory, psychomotor speed and executive function. The Short Form-36 (SF-36) was used to measure mental and physical HRQL, and the Hospital Anxiety and Depression Scale (HADS) to assess psychological distress.
Results: 33 survivors completed both exams (31 males, mean age 58.6 years, SD = 13). The OHCAs were witnessed and due to cardiac origins. Nine patients were awake at admission to the hospital. Longer coma duration was associated with poorer cognitive results. Memory impairments were the most common symptom. The mean changes and effect sizes indicated minor improvements in cognitive performance from 3 to 12 months (Hedges $g \leq .26$). Reliable change indices for an individual's results further confirmed the stability of the group statistics. The HADS scores showed increased depressive symptoms, and mental HRQL was reduced from 3 to 12 months. Higher reports of psychological distress were related to worse HRQL. Work participation increased. Better cognitive results at 3 months were correlated with better HRQL and return to work at 12 months.
Conclusions: The current data describe stability in results from 3 to 12 months. A worse cognitive performance at 3 months and higher reports of psychological distress were associated with lower HRQL.

Introduction

Cognitive dysfunction is estimated to occur in 30–50% of survivors of out-of-hospital cardiac arrest (OHCA) when measured with objective, performance-based neuropsychological tests in the first year after resuscitation.[1–3] Most frequently identified are problems with memory functions.[1–4] In addition to the hypoxic-ischemia caused by the circulatory arrest, other risk factors for cognitive decline exist in this patient group and include pre-existing cardiovascular burden and general critical illness.[1,5] Despite the existence of multiple risk factors for cognitive problems, cognitive decline is not regularly assessed and may go unrecognized in post-cardiac arrest care and follow-up.[3,6,7] Previous studies of cognitive outcomes have most often relied on a single time point of measurement.[3] Few previous prospective studies have assessed improvement in cognitive performance based on repeated neuropsychological testing of the same survivors over time.[3,8–12] It is generally suggested that cognitive recovery plateaus in the first 3 months after resuscitation and that early cognitive assessments approximate longer-term outcomes.[3] The aim of the present study was to assess improvement in cognitive functioning 3–12 months after resuscitation. Additionally, this study aimed to explore if worse cognitive functioning detected at 3 months anticipated worse functional prognosis in terms of poorer health related

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quality of life (HRQL), more psychological distress or not returning to work 1 year after an OHCA. Based on the results from previous studies, we expected little cognitive improvement beyond 3 months[3,10] but believed that lower cognitive performance could be associated with lower HRQL after 1 year.[6,10,13] We further expected that higher reported levels of psychological distress would negatively influence HRQL.[6,14]

Methods

The study was approved by the Regional Committee for Medical Research Ethics in North-Norway, institutional protocol number 2009/1395. Written consent was obtained from all participants.

Participants

We aimed to prospectively include all survivors of non-traumatic, normothermic OHCA of presumed cardiac origin, aged 18–85 years, who were discharged from the cardiac ward at the University hospital of North Norway between August 2010 and September 2013 and who were able to undergo a neuropsychological assessment 3 months after resuscitation. The hospital is a tertiary care center with an advanced cardiac ward serving smaller hospitals in a regional manner. According to hospital records, 197 survivors were treated for OHCA of any cause in the study period. Patients who died before or during hospital admission were not registered. Of these OHCAs, 129 were of cardiac origin. Participants had to be fluent Norwegian speakers, be living independently prior to cardiac arrest and have no history of psychiatric or neurologic disease or significant ongoing somatic disease, substance abuse or alcoholism. Fig. 1 shows a flow-chart starting with the total number of OHCA patients discharged alive from the cardiac ward during the study period who had an OHCA due to a presumed cardiac origin; the reasons for exclusion and loss to follow-up at both time points for assessment are also displayed.

Procedure

Survivors were invited to the hospital for an individual, outpatient, face-to-face follow-up assessment at 3 months (T1) and at 12 months (T2) post-OHCA that included performance-based neuropsychological tests and 2 self-report questionnaires: the Hospital Anxiety and Depression Scale (HADS)[15] and the Short Form (36) Health Survey (SF-36) version 1.2.[16] Experienced neuropsychologists administered and scored all tests according to standardized procedures. Tests and questionnaires were administered in one session at each time point. Age, education history, living situation and working status prior to cardiac arrest and at both follow-up time points were recorded from the patient interview. Information about their medical history and treatment variables were recorded from participants' medical journals at the hospital.

Description of the outcome measures

Neuropsychological tests

Details of the individual neuropsychological tests[17–22] are described in Supplementary Table 1. We selected tests that were representative of the cognitive functions described as being the most frequently impaired in OHCA survivors: declarative memory, executive function and psychomotor function.[2,3,11,13,23] The study was performed in a clinical setting, and thus only tests that are commonly applied in clinical practice were used. The tests selected have been widely used internationally and have been standardized to the Norwegian setting, with psychometric properties such as construct validity and test-retest reliability that have empirically been shown to be satisfactory to excellent. Published normative data from large groups of healthy individuals were used to score each test correcting for demographic variables.[17–22] The standardized test results were transformed to *Z*-scores:

$$\frac{\text{Patient score} - \text{normative mean score}}{\text{Normative standard deviation of the test}}$$

The tests were grouped into five cognitive domain composite scores based on construct validity. A mean *Z*-score for each domain was computed to both reduce the number of comparisons in the statistical analyses and to reduce the influence of possible idiosyncratic results that may have occurred by chance on single tests. A cut-off of ≤ -1.5 SD from the normative mean was used to characterize abnormal performance on each cognitive composite score.

Self-report questionnaires

The HADS is a brief self-report questionnaire that consists of 14 questions; 7 questions assess anxiety symptoms and 7 assess symptoms of depression (score 0–3 for each question), each scale having a maximum score of 21.[24] Scores at or above eight points on either the depression or anxiety scale are suggested to be clinically relevant.[14,24] The questionnaire is frequently used in studies of cardiac arrest survivors and has been shown to have sound psychometric properties.[14]

HRQL was measured with the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36 version 1.2), a generic HRQL measure that consists of 2 summary scales, a physical component scale (PCS) and a mental component scale (MCS), which are divided into 8 subscales: physical functioning (PF), physical role (RP), bodily pain (BP), general health (GH), mental health (MH), emotional role (RE), social function (SF) and vitality (VT).[16,25,26] The questionnaire asks patients about their perceptions of how their health status has interfered with their psychological, social and physical functioning in the previous 4 weeks. The participants' data were compared with age- and gender-corrected normative data from the general Norwegian population.[25] An online calculator for norm-based data scoring (http://www.sf36.org/nbscalc/index.shtlml) was applied for each survey, and the results were provided in normalized *T*-scores. When standardizing the scores according to the *T*-score distribution, the means were 50 and the standard deviations were 10 across all summary scales and subscales on the SF-36 in the comparator group. Thus, a direct comparison between the participants' *T*-scores and the age- and gender-corrected normative data in the general Norwegian population could be viewed in a single graph. Fig. 2 shows the standardized SF-36 results from the 33 participants at both time points of assessment. $T < 40$ on any of the scales is suggested to represent HRQL below the normal range.[26]

Statistical analyses

Statistical analyses were performed in IBM SPSS (version 22).

Missing data at T1 were found in three participants on the Rey Complex Figure and in two participants on the Grooved Pegboard tests. At T2, missing data were found for one participant on the Grooved Pegboard test and in two participants on the Word-Fluency Test. In the HADS data, two participants had missing data. All missing data were replaced by the series mean.

Before performing inferential statistics, all continuous variables were examined for normality by the Shapiro–Wilk test and by visual inspection of the *Q*–*Q* plots and box-plots of the distributions. Continuous variables were analyzed by parametric tests, as none of the continuous data were significantly different from a normal distribution.

Statistical group comparisons were performed by one-way analysis of variance (ANOVA). To test whether the mean of the continuous data differed from normative data, one-sample *t*-tests were