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Clinical Paper

# The influence of age and chronic medical conditions on neurological outcomes in out of hospital cardiac arrest

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ABSTRACT

*Aim:* It is unknown whether older patients with out of hospital cardiac arrest (OHCA) have worse outcomes because of aging itself, or because age can be a marker for overall health status. We aimed to study the prognostic utility of age and pre-arrest comorbidities.
*Methods:* We conducted a retrospective cohort study, reviewing electronic health records of all adults treated for non-traumatic OHCA in the University of Michigan Emergency Department ($N = 588$). Primary covariates included age, Charlson Comorbidity Index (CCI), and a combined Charlson-age index. The primary dichotomized outcome was favorable neurological outcome (cerebral performance category, 1–2), evaluated by logistic regressions.
*Results:* Dementia ($p = 0.01$), witnessed arrest ($p = 0.03$), bystander CPR ($p < 0.001$), presenting rhythm ($p < 0.001$), and mild therapeutic hypothermia ($p < 0.001$) were associated with the primary outcome. Increasing age (unadjusted OR for each decade of life, 95% CI: 0.78, 0.70–0.88; adjusted 0.79, 0.67–0.94) was negatively associated with likelihood of a favorable neurological outcome. CCI and combined Charlson-age index significantly predicted outcome in the unadjusted, but not adjusted analysis. Composite variables were stronger predictors in patients with shockable than non-shockable presenting rhythms (interaction terms: age and rhythm [$p = 0.004$], CCI and rhythm [$p = 0.01$]).
*Conclusion:* Age, but not CCI, was significantly associated with less favorable neurological outcomes in patients with OHCA after adjusting important covariates. Age appears to be an independent predictor of prognosis rather than a marker for comorbidity.



## 1. Introduction

Over 420,000 out of hospital cardiac arrests (OHCA) occur each year in the US, with an estimated overall survival to hospital discharge of 10.4% for EMS-treated non-traumatic arrests.[1] Given a high degree of neurological morbidity and mortality,[2] considerable attention continues to focus on accurate multimodal assessment of prognosis following resuscitation from OHCA.[3–9]

Baseline pre-arrest health status, however, has frequently been neglected in studies of prognosis in comatose survivors of cardiac arrest. Some studies have examined the impact of specific comorbidities[10,11,14,31,32] or composite scales[10–12] on short term survival after OHCA. However, none fully captured functional or neurological outcomes beyond simply survival or adequately account for mild therapeutic hypothermia (MTH). Furthermore, although heterogeneous studies have suggested that age has predictive value, evidence for the independent predictive values of comorbidities (i.e. physiological age) and chronological age are scarce.[13]

We therefore conducted the present study to evaluate the independent predictive values of pre-arrest patient characteristics on neurological outcomes. We hypothesized that both overall physiological age measured by a summed comorbidity score and chronological age would contain independently predictive prognostic information.

## 2. Methods

### 2.1. Study design

This was an observational retrospective cohort study.[14] Patients were classified by their Charlson Comorbidity Index (CCI),[15,16] decade of life, and a combined Charlson-age index.

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### 2.2. Patient selection

Electronic health records were screened for all patients presenting to the University of Michigan Emergency Department (ED) with diagnosis coded as cardiac arrest between 1/1/2005 and 9/14/2012. We also screened patients on an independent log of targeted temperature management (TTM) equipment use. Patients were excluded if they were less than 18 years old at the time of arrest or had a traumatic etiology.

### 2.3. Mild therapeutic hypothermia

Hypothermia at our institution was accomplished via endovascular cooling (Innercool-Philips, San Diego, CA) for 24 h at a target of 33 °C followed by controlled rewarming over 24 h back to normothermia. Implementation of the hypothermia program at our institution began in July 2006. Non-binding institutional eligibility guidelines for cooling include all comatose patients with return of spontaneous circulation (ROSC) regardless of rhythm and etiology.

### 2.4. Data collection and outcome assessment

This project was reviewed and determined exempt by the University of Michigan Institutional Review Board (HUM00018775). Data collection was modeled after Utstein recommendations[17] and reported according to accepted standards in chart review research.[18]

All clinical parameters and baseline comorbidities were abstracted from University of Michigan electronic medical health records by a single reviewer (ST) using an explicit chart abstraction form. The reviewer was not blinded to the study purpose during data collection. Details regarding demographics, resuscitation, hypothermia, and discharge vital status were determined. Neurological outcomes were determined from the electronic health record by at least two independent reviewers (ST, RS, and TS and when discordant resolved by consensus or adjudicated by the third reviewer.

Neurological outcomes were characterized by Cerebral Performance Category (CPC)[19–21] dichotomized as favorable (CPC 1–2, i.e. no symptoms and/or independence) or unfavorable (CPC 3–5, i.e. dependent, comatose, or dead). Our primary outcome occurred at hospital discharge, with secondary analyses at 6–12 months post-discharge. Outcomes were determined by reviewing all relevant health records including inpatient and outpatient physician and physical/occupational therapy evaluations. Determination of CPC from chart review has been previously determined to have moderately good correlation with that determined by patient interview.[22]

The primary covariates included CCI, age at the time of arrest, and a combined Charlson-age index. The CCI is a commonly used summed score which assigns severity-weighted points for chronic health conditions. It was originally created to assess mortality risk in a general medical inpatient service at the New York Hospital-Cornell Medical Center, tested in a cancer population at Yale New Haven Hospital, and validated in a general surgical cohort.[15,16] The comorbidities included in the calculation of CCI and disease severity weighting scheme can be found in Charlson et al., 1987.[16] Our Table 1 also lists these elements and weighting. The combined Charlson-age index is calculated from the CCI plus 1 point for each decade of life after the fifth decade. Comorbidities were counted if any previous mention of each specific disease was listed in a patient's medical record on either the arrest admission or prior medical records at the University of Michigan.

Data were collected and managed using REDCap (Research Electronic Data Capture; Vanderbilt University, Nashville, TN).[23]

### 2.5. Statistical analysis

Descriptive statistics were used to characterize the patient cohort. Continuous variables were described using medians and interquartile ranges. Categorical variables were described as frequencies and percentages within each group.

We first performed bivariate analysis examining whether individual baseline and arrest-related factors were associated with the primary outcome using logistic regressions. $p$-Values were obtained via Chi-squared or Fisher's exact tests for categorical variables and logistic regressions for continuous variables.

We first categorized and analyzed the primary covariates using 1-sided Cochrane-Armitage tests for trend, given our hypothesis of a 1-sided trend. We then analyzed them as continuous variables using logistic regressions. Dichotomous CPC was modeled as the outcome. Unadjusted models included only a single continuous main covariate: either age (years), CCI, or combined age-Charlson index. We then adjusted in two steps: (1) age was adjusted for CCI and CCI adjusted for age, and (2) adjusted for all potentially relevant measured variables. Interactions between the main variables and other important variables were evaluated, and we performed various sensitivity analyses using our secondary outcome and incorporating withdrawal of care into our regressions.

All analyses were completed using SAS version 9.3 (Cary, NC). $p$-Values <0.05 were considered significant.

## 3. Results

### 3.1. Baseline characteristics

Six hundred thirty-eight adult patients were treated for OHCA in our ED during the study period. Forty-eight had a traumatic etiology and were excluded.

Baseline characteristics of the remaining 590 are displayed in Table 1. A hospital discharge CPC could be determined in 588 (99.7%), and a long term (6–12 month) CPC in 558 (95%).

### 3.2. Association of individual variables with neurological outcome

Of the 588 included patients, 352 (60%) had any ROSC, 121 (21%) survived to hospital discharge, and 98 (17%) had a favorable CPC at hospital discharge.

Table 1 displays the association between each baseline characteristic and our primary outcome. Individual variables which significantly predicted more favorable outcomes included younger age, absence of underlying dementia, witnessed arrest, receiving bystander CPR, shockable presenting rhythm, receiving MTH, and cardiovascular etiology. No other individual baseline comorbidity was significantly associated with outcomes.

### 3.3. Association of composite variables with neurological outcome

Fig. 1 displays the proportion of patients with favorable outcomes according to (a) age, (b) CCI, and (c) combined Charlson-age index. Both increasing decade of life ($p < 0.001$) and combined Charlson-age index ($p < 0.001$) predicted significantly worse outcomes, while categorized CCI alone was of borderline significance ($p = 0.06$).

Analyzed as continuous variables, decade of life remained significantly associated with worse outcomes in an unadjusted model (OR for each decade, 95% CI: 0.78, 0.70–0.88), when adjusting only for CCI (0.80, 0.71–0.90), and in the fully adjusted model (0.79, 0.67–0.94). Both CCI and the combined Charlson-age index were significantly negatively associated with favorable neurological outcome in unadjusted but not adjusted analysis (Table 2a).