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Association between clinical examination and outcome after cardiac arrest☆

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ABSTRACT

Background: Neurologic prognostication after cardiac arrest relies on clinical examination findings derived before the advent of therapeutic hypothermia (TH). We measured the association between clinical examination findings at hospital arrival, 24, and 72 h after cardiac arrest in a modern intensive care unit setting.

Methods: Between 1/1/2005 and 3/31/2009, hospital charts were reviewed in 272 subjects for neurologic examination findings (Glasgow Coma Score – motor examination, pupil response, corneal response) at hospital arrival, 24, and 72 h following cardiac arrest. Primary outcome was survival to hospital discharge. Secondary outcome was "good outcome," defined as discharge to home or acute rehabilitation facility.

Results: Mean age was 61 years; 155 (57%) were male. Most were treated with TH ($N = 161$; 59%) and 100 subjects (37%) were in ventricular fibrillation/ventricular tachycardia. Out-of-hospital cardiac arrest was common ($N = 169$; 62%). Ninety-one (33%) survived, with 54 (20%) experiencing a good outcome.

In subjects with a GCS Motor score ≤3 at 24 and 72 h survival was 17% (13/76; 95% CI 7.9–26.2%) and 20% (6/27; 95% CI 6.3–33.6%), respectively. Subjects with a GCS Motor score ≤2 at 24 and 72 h survived in 14% (9/66; 95% CI 4.6–22.6%) and 18% (6/33; 95% CI 3.5–32.8%), respectively. Absent pupil reactivity on arrival did not exclude survival (7/65; 11%; 95% CI 2.4–19%). A lack of pupil reactivity or corneal response at 72 h was associated with death (pupil: 0/17; 95% CI 0, 2.9%; corneal: 0/21; 95% CI 0, 2.4%).

Conclusions: GCS Motor score ≤3 or ≤2 at 24 or 72 h following cardiac arrest does not exclude survival or good outcome. However, absent pupil or corneal response at 72 h appears to exclude survival and good outcome.

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1. Introduction

Cardiac arrest results in approximately 350,000 deaths each year.[1] Failure to awaken from subsequent coma is common and a leading cause of death in post-cardiac arrest patients admitted to the intensive care unit (ICU) setting.[2] Clinical neurologic examination is the primary tool for predicting prognosis after cardiac arrest.[3] However, the reference data to which patients are compared were obtained prior to modern critical care.[4–6]

The use of therapeutic hypothermia (TH) and a comprehensive care plan after cardiac arrest improves neurologic outcomes.[7–10] Because of these recent innovations in care, the predictive value of specific parts of the clinical examination should be re-evaluated using more recent cohorts.[11,12] It is essential to determine whether TH, which may improve the natural history of recovery after cardiac arrest, alters the relationship between these clinical findings and outcome.

Prior literature recommends attention to pupil response, corneal reflexes, and motor response to stimulation for determining prognosis after cardiac arrest.[3,4,6] The greatest predictive value for these clinical findings has been reported at hospital arrival, 24, and 72 h after admission. To reassess the current predictive value of these findings, data were obtained from a modern cohort of subjects with coma after cardiac arrest, including subjects treated with therapeutic hypothermia. This study measured the association between survival and the presence of pupil response, corneal reflex, and motor response in comatose subjects at hospital arrival, 24, and 72 h after cardiac arrest. Secondarily, this study examined whether these relationships differ according to the use of TH.

2. Methods

2.1. Study design

We conducted a retrospective chart review of consecutive patients admitted after cardiac arrest between January 1, 2005 and

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March 31, 2009. Charts were reviewed to determine neurologic examination findings and outcomes following cardiac arrest.

2.2. Study setting

The study was conducted at a single urban academic medical center that serves as a referral center for over four million people. Cardiac arrest was defined as a patient who required cardiopulmonary resuscitation or a rescue shock for a pulseless rhythm. All patients >18 years of age were eligible. In 2007, this facility added a specialized post-cardiac arrest comprehensive care plan including TH, aggressive coronary revascularization, rehabilitation, and secondary prevention for all patients admitted after resuscitation from cardiac arrest.[10] TH is offered to patients regardless of location of arrest or primary rhythm of arrest. A post-cardiac arrest care clinical service was also implemented in 2007 to ensure the care plan was delivered to eligible patients. Utilization of TH increased from <5% to >90% of eligible cases between 2005 and 2009.

2.3. Standard protocol approvals

This study was approved by the University of Pittsburgh Institutional Review Board.

2.4. Methods of measurement

We retrospectively assessed hospital charts for neurologic examination findings (Glasgow Coma Score (GCS) – motor examination, pupil response, corneal response) at hospital arrival, 24, and 72 h following cardiac arrest. Charts were included regardless of TH use. The physical examination findings were preferentially obtained from one of the attending cardiac arrest physicians (JCR, FXG, and CWC) directing the post-cardiac arrest care in 134 subjects. These physicians focused their neurologic exam based on the criteria in the AAN 2006 guidelines and derived from the seminal work by Levy et al.[4,6] Their exams were used for all subjects receiving therapeutic hypothermia and 12 subjects not receiving therapeutic hypothermia. Data from patients under sedation, paralyzed, or dead at the time point were considered not valid. Data were also considered not valid if it could not be determined that the patient was examined without sedation or paralysis from the attending physician or ICU nursing note. In our facility, the majority of post-cardiac arrest patients receive diprivan for sedation. Examinations were completed when propofol had been stopped for 20–30 min as part of either the attending physician's clinical examination or during the daily "interruption of sedation" completed by the ICU nurse. In this protocol, the sedation is stopped until the patient is at a Ramsay Scale of 2 or the patient is unable to tolerate, defined as an increase in heart rate, respiratory rate or blood pressure more than 20%, pulse oximetry below 90%, respiratory rate >30/min, elevated airway pressures, or intracranial pressure >20 mm Hg. Patient age, sex, location of arrest, primary rhythm of arrest, use of therapeutic hypothermia, survival, and good outcome were also abstracted. A list of standard clinical examination features was reliably abstracted by two authors (JS and MW) with good to excellent agreement at all time intervals (kappa values ranging between 0.74 and 1.0 for arrival data, 1.0 for 24 h data, and 0.63–1.0 for 72 h data).

2.5. Outcome measures

Our primary outcome was survival to hospital discharge. A secondary measure was "good outcome," defined as discharge to home or acute rehabilitation facility. Good outcome is an approximation of Cerebral Performance Category of 1 or 2.[10]

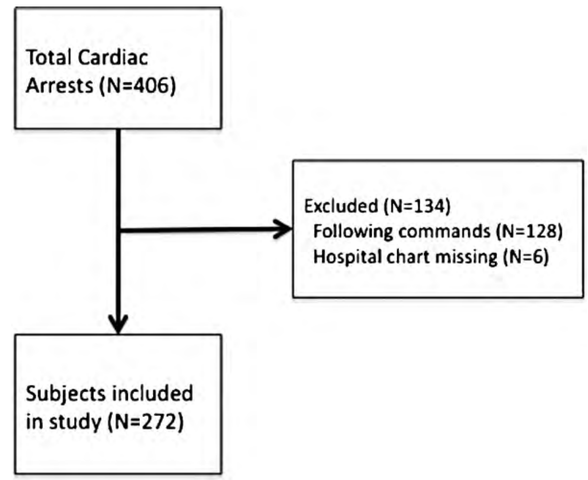

Fig. 1. Cardiac arrest patients between 1/1/2005 and 3/30/2009.

2.6. Data analysis

Data are presented using descriptive statistics. The primary analysis was to determine the association between 24 h GCS Motor score, 72 h GCS Motor score, initial pupil examination, 72 h pupil examination, 72 h corneal examination and survival. Data were analyzed using the Levy criteria of GCS Motor of $\leq$3 as well as the AAN 2006 guidelines using a GCS Motor of $\leq$2 as the cutpoint. Odds ratios were used to describe the association between each examination and survival. Secondary analyses were the association between clinical examination findings and good outcome in the subsets of patients with or without TH. Bonferroni correction was used for multiple comparisons. Thus, the p value for significance was 0.005 for comparing patients treated with or without TH. The association of each finding with good outcome was determined. Data were analyzed using STATA (version 9.2, College Station, TX).

3. Results

A total of 406 subjects were identified during this interval. Of these, 128 subjects were excluded because they were awake on arrival, and an additional 6 subjects were excluded due to a missing hospital chart. This resulted in a total of 272 subjects for analysis (Fig. 1).

Mean age was 61 (SD 16) years of age and the majority (N = 155; 57%) were male (Table 1). Only 100 subjects (37%) were in ventricular fibrillation/ventricular tachycardia. Out-of-hospital cardiac arrest was common (N = 169; 62%) and most (N = 161; 59%) received TH. Overall, 91 (33%) subjects survived, with 54 (20%) experiencing a good outcome. Subjects with missing data at 24 and 72 h were more likely to have received TH. Subjects dead at 72 h were less likely to have VF/VT as the primary rhythm of arrest (Table 1). The rate of death within 72 h was not different over time (2005 –38%; 2006 – 29%; 2007 – 29%; 2008 – 28%; 2009 – 40%; p = 0.65).

Neither of the GCS Motor exam findings studied at 24 or 72 h was universally predictive of mortality (Tables 2 and 3). In subjects with a GCS Motor score $\leq$3 at 24 h survival was 17% (13/76; 95% CI 7.9–26.2%) and 20% (8/40; 95% CI 6.3–33.6%) at 72 h. Similarly, in subjects with a GCS Motor score $\leq$2 at 24 h survival was 14% (9/66; 95% CI 4.6–22.6%) and 18% (6/33; 95% CI 3.5–32.8%) at 72 h. A lack of pupil reactivity on arrival did not exclude survival (7/65; 11%; 95% CI 2.4–19%). Death was associated with a lack of pupil reactivity at 72 h (0/17 survival; 95% CI 0, 2.9%) or a lack of corneal response at 72 h (0/21 survival; 95% CI 0, 2.4%).

Table 1
Demographics of initial, 24, and 72-h cohorts. Excluded cases were sedated, paralyzed or dead prior to examination and not included in the analysis for that time point. OHCA, out-of-hospital cardiac arrest; VT/VF, ventricular tachycardia/ventricular fibrillation; PEA, pulseless electrical activity.

		Time 0		24 h			72 h		
	Cohort (*N* = 272)	Valid data (*N* = 226)	Sedated/paralyzed (*N* = 46)	Valid data (*N* = 235)	Sedated/paralyzed (*N* = 34)	Dead (*N* = 3)	Valid data (*N* = 172)	Sedated/paralyzed (*N* = 17)	Dead (*N* = 83)
Age in years (SD)	61 (16)	61 (16)	61 (17)	61 (17)	61 (15)	76 (18)	60 (15)*	52 (17)*	64 (18)*
Male	155 (57%)	124 (55%)	31 (67%)	132 (56%)	21 (62%)	2 (67%)	103 (60%)	11 (65%)	41 (49%)
OHCA	169 (62%)	137 (61%)	32 (70%)	143 (61%)	24 (71%)	2 (67%)	103 (60%)	11 (65%)	55 (66%)
Hypothermia	161 (59%)	122 (54%)	38 (83%)	126 (54%)*	34 (100%)*	1 (33%)*	95 (56%)*	17 (100%)*	47 (57%)*
VF/VT	100 (37%)	78 (35%)	22 (48%)	85 (36%)	15 (44%)	0 (0%)	78 (45%)*	7 (41%)*	15 (18%)*
PEA	73 (27%)	64 (28%)	9 (20%)	67 (28%)	5 (14%)	1 (33%)	38 (22%)	4 (24%)	31 (37%)
Asystole	62 (23%)	55 (24%)	7 (15%)	53 (23%)	7 (21%)	2 (67%)	35 (21%)	5 (29%)	22 (27%)
Unknown	37 (13%)	29 (13%)	8 (17%)	30 (13%)	7 (21%)	0 (0%)	21 (12%)	1 (6%)	15 (18%)
Survival to hospital discharge	91 (33%)	74 (33%)	17 (37%)	79 (34%)	12 (35%)	0 (0%)	85 (49%)	5 (29%)	0 (0%)
Good Outcome	54 (20%)	44 (19%)	10 (22%)	50 (21%)	5 (12%)	0 (0%)	52 (30%)	2 (12%)	0 (0%)

* $p < 0.05$ between valid data, sedated/paralyzed and dead groups.

Table 2
Outcomes in normothermia patients by (A) GCS Motor, (B) pupil response, and (C) corneal response at arrival, 24, and 72 h following cardiac arrest.

	GCS Motor >3	GCS Motor ≤3	Odds ratio (95% CI)	GCS Motor >2	GCS Motor ≤2	Odds ratio (95% CI)
(A)						
24 h Survival	35/93 (38%; 95% CI 27, 43%)	3/16 (19%; 95% CI 0, 41%)	2.61 (0.70, 9.82)	36/94 (38%; 95% CI 28, 49%)	2/15 (13%; 95% CI 0, 34%)	4.03 (0.86, 18.92)
Good outcome	22/93 (24%; 95% CI 14, 33%)	2/16 (13%; 95% CI 0, 32%)	2.11 (0.45, 10.00)	23/94 (24%; 95% CI 15, 34%)	1/15 (7%; 95% CI 0, 23%)	4.54 (0.57, 36.39)
72 h Survival	33/63 (52%; 95% CI 39, 66%)	4/12 (33%; 95% CI 2, 64%)	2.2 (0.60, 8.06)	33/65 (51%; 95% CI 38, 64%)	4/10 (40%; 95% CI 5, 75%)	1.55 (0.40, 6.00)
Good outcome	22/63 (35%; 95% CI 22, 47%)	2/12 (17%; 95% CI 0, 42%)	2.68 (0.54, 13.34)	22/65 (34%; 95% CI 22, 46%)	2/10 (20%; 95% CI 0, 50%)	2.05 (0.40, 10.47)

	Pupil reactive	Pupil not reactive	Odds ratio (95% CI)
(B)			
Arrival Survival	21/37 (57%; 95% CI 39, 74%)	2/14 (14%; 95% CI 0, 36%)	7.88 (1.54, 40.28)
Good outcome	17/37 (46%; 95% CI 29, 63%)	1/14 (7%; 95% CI 0, 24%)	11.05 (1.31, 93.38)
72 h Survival	22/39 (56%; 95 CI 40, 73%)	0/1 (0%; 95% CI 0, 50%)	–
Good outcome	17/39 (44%; 95% 27, 60%)	0/1 (0%; 95% CI 0, 50%)	–

	Corneal reactive	Corneal not reactive	Odds ratio (95% CI)
(C)			
72 h Survival	22/39 (56%; 95% 40, 73%)	0/1 (0%; 95% CI 0, 50%)	–
Good outcome	17/39 (44%; 95% CI 27, 60%)	0/1 (0%; 95% CI 0, 50%)	–

Table 3
Outcomes in hypothermia patients by (A) GCS Motor, (B) pupil response, and (C) corneal response at arrival, 24, and 72 h following cardiac arrest.

	GCS Motor >3	GCS Motor ≤3	Odds ratio (95% CI)	GCS Motor >2	GCS Motor ≤2	Odds ratio (95% CI)
(A)						
24 h						
Survival	31/66 (47%; 95% CI 34, 60%)	10/60 (17%; 95% CI 6, 27%)	4.43 (1.92, 10.19)	34/75 (45%; 95% CI 33, 57%)	7/51 (14%; 95% CI 3, 24%)	5.21 (2.08, 13.05)
Good outcome	20/66 (30%; 95% CI 18, 42%)	6/60 (10%; 95% CI 2, 18%)	3.83 (1.42, 10.33)	22/75 (29%; 95% CI 18, 40%)	4/51 (8%; 95% CI 0, 16%)	4.88 (1.57, 15.18)
72 h						
Survival	44/69 (64%; 95% CI 52, 76%)	4/28 (14%; 95% CI 0, 29%)	10.56 (3.29, 33.92)	46/74 (62%; 95% CI 50, 74%)	2/23 (9%; 95% CI 0, 22%)	17.25 (3.76, 79.23)
Good outcome	26/69 (38%; 95% CI 26, 50%)	2/28 (7%; 95% CI 0, 18%)	7.86 (1.72, 35.88)	27/74 (36%; 95% CI 25, 48%)	1/23 (4%; 95% CI 0, 15%)	12.64 (1.61, 99.07)
	Pupil reactive	Pupil not reactive	Odds ratio (95% CI)			
(B)						
Arrival						
Survival	27/56 (48%; 95% CI 34, 62%)	5/51 (10%; 95% CI 1, 19%)	8.57 (2.96, 24.76)			
Good outcome	17/56 (30%; 95% CI 17, 43%)	2/51 (4%; 95% CI 0, 10%)	10.68 (2.33, 49.04)			
72 h						
Survival	41/56 (73%; 95% CI 61, 86%)	0/16 (0%; 95% CI 0, 3%)	–			
Good outcome	26/56 (46%; 95% CI 32, 60%)	0/16 (0%; 95% CI 0, 3%)	–			
	Corneal reactive	Corneal not reactive	Odds ratio (95% CI)			
(C)						
72 h						
Survival	42/53 (79%; 95% CI 67, 91%)	0/20 (0%; 95% CI 0, 3%)	–			
Good outcome	26/53 (49% 95% CI 35, 63%)	0/20 (0%; 95% CI 0, 3%)	–			

A total of 111 subjects did not receive TH (Table 2). Neither a GCS Motor score >3 at 24 h (odds ratio [OR] 2.61; 95% CI 0.70–9.82) nor 72 h (OR 2.2; 95% CI 0.60–8.06) predicted survival. Similarly, a GCS Motor score >2 at 24 h (OR 4.03; 95% CI 0.86–18.92) and 72 h (OR 1.55; 95% CI 0.40–6.00) did not predict survival. A pupil response at hospital arrival was associated with survival (OR 7.88; 95% CI 1.54–40.28). The single subject without pupil response and without corneal response at 72 h did not survive.

A total of 161 subjects were treated with TH (Table 3). A GCS Motor score >3 at 24 and 72 h predicted survival (OR 4.43; 95% CI 1.92–10.19 at 24 h and OR 10.56; 95% CI 3.29, 33.92 at 72 h). A GCS Motor score >2 at 24 and 72 h similarly predicted survival (OR 5.21; 95% CI 2.08–13.05 at 24 h and OR 17.25; 95% CI 3.76–79.23 at 72 h). A pupil response on arrival was also associated with survival (OR 8.57; 95% CI 2.96–24.76).

Association between good outcome and examination findings did not differ between subjects treated with and without TH. The proportion of good outcome did not differ between normothermia and TH groups for subjects with pupil response on arrival (present: Chi square 1.06, $p = 0.30$; absent: Chi square 0.23, $p = 0.63$) or GCS Motor score at 24 h (>3: Chi square 0.16, $p = 0.69$; ≤3 Chi square 0.07, $p = 0.80$; >2 Chi square 0.29, $p = 0.59$; ≤2 Chi square 0.02, $p = 0.89$).

Regardless of TH use, at 72 h the association between good outcome and GCS Motor score did not differ (>3 Chi square 0.05, $p = 0.82$; ≤3 Chi square 0.67, $p = 0.41$). TH use did not alter the association between good outcome and intact pupil response (Chi square 0.03, $p = 0.87$) or intact corneal response (Chi square 0.10, $p = 0.75$). Finally, TH did not affect the association between good outcome and GCS Motor score (>2 Chi square 0.05, $p = 0.82$; ≤2 Chi square 1.64, $p = 0.20$).

A lack of pupil response on arrival did not exclude good outcome in either the TH or normothermia cohorts (Tables 2 and 3). Neither a GCS Motor score ≤3 nor ≤2 excluded good outcome in either cohort. Finally, a lack of pupil response or lack of corneal response at 72 h was associated with uniformly poor outcomes.

4. Discussion

This study reported the relationship between clinical examination findings customarily used to establish prognosis after cardiac arrest and survival in a modern cohort of patients. None of the clinical exam findings tested at arrival or 24 h were 100% predictive of death. Based on these data, the physical exam is insufficient for prognostication after cardiac arrest at 24 h. Nether GCS Motor score ≤3 or ≤2 at 72 h excluded survival. These data suggest that the motor examination is less useful than proposed in the landmark study by Levy and existing practice guidelines.[4,6]

In the absence of sedation, a lack of pupil or corneal responses at 72 h is highly predictive for poor neurologic outcome. This holds true for both the normothermic and hypothermic cohorts of patients treated in our center. Our data support the practice guidelines recommendation that absence of brainstem function should prompt consideration of brain death.[6] Ominously, it may indicate that many patients are given insufficient time to declare themselves after suffering a significant ischemic brain injury.

We note that the GCS Motor score did not exclude survival or good outcome in either the normothermic or hypothermic cohorts. This finding suggests that differences between our data and prior studies[4] are a function of modern ICU care rather than just therapeutic hypothermia. The point estimates and wide confidence intervals for motor exam at 72 h are significantly different from the classic data.[4] This change in prognostic value of a specific clinical examination finding illustrates the need to recalibrate scales and decision rules because of secular trends in care.[13]

The limited certainty of neurological examination alone to predict survival or good outcome after cardiac arrest supports recommendations that a multimodal prognostic workup may be necessary.[11,12] For example, a combination of clinical examination, somatosensory evoked potentials, magnetic resonance imaging, electroencephalography, and serum markers of neuronal injury may provide greater certainty in assessment.[14–18]

5. Limitations

These retrospective data were obtained from one tertiary care facility with a standardized post-cardiac arrest care plan provided by a dedicated multi-disciplinary team since 2007. The clinicians providing post-arrest care use a multimodal workup including electroencephalography, computerized tomography, magnetic resonance imaging, clinical examination findings, and somatosensory evoked potentials to determine neurologic viability. Prior to 2007, the prognostic workup of these patients was variable. We note that the rate of death prior to 72 h of hospitalization was not different during the course of this study suggesting that early deaths due to neurologic injury are either constant over time or may be independent of neurologic injury. Regardless, the variation in prognostic workup likely reflects many facilities and thus improves generalizability.

6. Conclusions

In non-sedated patients, neither a GCS Motor score $\leq$3 nor $\leq$2 at 24 or 72 h following cardiac arrest excludes survival or good outcome in the modern ICU era. However, lack of pupil or corneal response at 72 h appears to exclude survival and good outcome. Survival in the modern ICU era is higher than in prior cohorts.

Conflict of interest

The authors have no conflict of interest to report.

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