Journal meeting

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DATE:2011/12/5

An early, novel illness severity score to predict outcome after cardiac arrest

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Introduction

- Syndrome of post-cardiac arrest illness
  - consisting of several distinct patho-physiological changes.
- Severity of illness is an important **determinant** of the response to therapeutic interventions

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Introduction

- Classifying post-cardiac arrest patients with:
  - **Historical**: initial cardiac rhythm,
  - **Event-related**: witnessed collapse or location of collapse
- These classifications suffer from modest reliability and weak association with in-hospital clinical course

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Introduction

- Data obtained after **ROSC** (restoration of spontaneous circulation) and prior to reaching target temperature
  - stratify post-cardiac arrest patients into clinically meaningful illness severity categories
  - Such categories permit tailoring of therapy for post-arrest patients

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Method

- Subjects were adults (≥18 years) admitted to the emergency department or intensive care unit at a single tertiary care center after ROSC following cardiac arrest

Method

- Cardiac arrest was defined as receiving chest compressions or rescue shock by a professional healthcare provider
  - Included both in-hospital cardiac arrest (IHCA) and out-of hospital cardiac arrest (OHCA)
- Cardiac arrests occurring in the emergency department were classified as IHCA

Method

- Multi-disciplinary post-cardiac arrest care plan
  - **Therapeutic hypothermia (TH)**
  - **Optimize cerebral perfusion**
  - **Maintain a urine output of ≥ 0.5 mL/kg/h**
  - **Emergent coronary angiography**

Method

- **Therapeutic hypothermia (TH)**
  - The protocol involves rapid induction of TH to a goal temperature of 33 C for 24 h followed by gradual rewarming (0.25 C) to normothermia

Method

- **Optimize cerebral perfusion**
  - Mean arterial blood pressure is targeted to ≥ 80 mmHg
  - Ventilator settings are titrated for a pCO2 of 40

- **Maintain a urine output of ≥ 0.5 mL/kg/h**
  - Fluid infusion along with vasopressor or inotropes

Method

- **Emergent coronary angiography**
  - Patients with STEMI or a new left-bundle branch block on EKG
  - Patients with a history and symptoms consistent with acute myocardial infarction, cardiogenic shock, or focal wall motion abnormality on echocardiogram

Method

Characteristics of subjects deriving category of arrest. Therapeutic hypothermia achieved delineates the group where temperature ≤34 °C was achieved.

	Included (N = 457)	Excluded (N = 38)
Age, in years (SD)	61 (16)	61 (14)
Male sex	259 (57%)	25 (66%)
OHCA*	253 (55%)	9 (24%)
Rhythm*		
VF/VT	185 (41%)	8 (21%)
PEA	131 (29%)	9 (24%)
Asystole	88 (19%)	11 (29%)
Unknown	52 (11%)	10 (26%)
Year*		
2005	64 (14%)	4 (10%)
2006	86 (19%)	8 (21%)
2007	82 (18%)	2 (6%)
2008	103 (22%)	20 (53%)
2009	122 (27%)	4 (10%)
Therapeutic hypothermia intended	221 (48%)	21 (55%)
Therapeutic hypothermia achieved	202 (44%)	13 (34%)
Coma on arrival (GCS <9)*	287 (62%)	31 (82%)
Coronary angiography*	160 (45%)	3 (12%)
LOS (IQR)	7 (4, 15)	10 (4, 21)
Survival	213 (47%)	19 (50%)
Good outcome	144 (32%)	7 (18%)

Method: SOFA score

- **Organ system dysfunction** was determined using the individual organ dysfunction subscales of the Serial Organ Function Assessment (SOFA) scale

Method: SOFA score

- The SOFA score ranges from 0 to 4 in each of the following organ systems:
  - **Cardiovascular**
  - **Respiratory**
  - **Nervous**
  - **Liver**
  - **Coagulation**
  - **Renal**

Method: SOFA score

Cardio Vascular System

Mean Arterial Pressure OR administration of vasopressors required	SOFA score
MAP < 70 mm/Hg	1
dop <= 5 or dob (any dose)	2
dop > 5 OR epi <= 0.1 OR nor <= 0.1	3
dop > 15 OR epi > 0.1 OR nor > 0.1	4

(vasopressor drug doses are in mcg/kg/min)

Nervous System

Glasgow coma scale	SOFA score
13 – 14	1
10 – 12	2
6 – 9	3
< 6	4

Respiratory System

PaO_2/FiO_2 (mmHg)	SOFA score
< 400	1
< 300	2
< 200 **and** mechanically ventilated	3
< 100 **and** mechanically ventilated	4

Method: SOFA score

Nervous System

Glasgow coma scale	SOFA score
13 – 14	1
10 – 12	2
6 – 9	3
< 6	4

Liver

Bilirubin (mg/dl) [mmol/L]	SOFA score
1.2 – 1.9 [>20.5 - 32.5]	1
2.0 – 5.9 [34.2 - 100.9]	2
6.0 – 11.9 [102.6 - 203]	3
> 12.0 [>205]	4

Renal System

Creatinine (mg/dl) [mmol/L] (or urine output)	SOFA score
1.2 – 1.9 [92 - 145]	1
2.0 – 3.4 [152 - 259]	2
3.5 – 4.9 [267 - 374] (or < 500 ml/d)	3
> 5.0 [>382] (or < 200 ml/d)	4

Coagulation

Platelets×10^3/mcl	SOFA score
< 150	1
< 100	2
< 50	3
< 20	4

Method: SOFA score

- **Organ failure** was defined as a score ≥3 (range 0–4) on one subscale of the SOFA
- **MOF** defined as a score of ≥3 on three or more subscales during the first 72 h of hospitalization
- Baseline organ dysfunction was determined using data obtained within the first 6 h after cardiac arrest

Method: FOUR score

- **Neurological status** was rated for subjects by using the Full Outline of Unresponsiveness (FOUR) score

Method: FOUR score

Eye Response	Findings	Score
	eyelids open and tracking, or blinking on command	4
	eyelids open but not tracking	3
	eyelids closed but open to loud voice	2
	eyelids closed but open to pain	1
	eyelids closed with pain	0

Motor Response	Findings	Score
	makes sign (thumbs-up, fist, other)	4
	localizing to pain	3
	flexion response to pain	2
	extension response to pain	1
	no response to pain	0
	generalized myoclonus status	0

Method: FOUR score

Pupil Reflexes	Corneal Reflexes	Cough	Brainstem Score
present	present	present	4
one pupil wide and fixed	present	present	3
absent	present	NA	2
present	absent	NA	2
absent	absent	present	1
absent	absent	absent	0

Intubation	Breathing		Respiratory Score
not intubated	regular		4
not intubated	Cheyne-Stokes		3
not intubated	irregular		2
not intubated	apnea		0
intubated	above ventilator rate		1
intubated	breathes at ventilator rate		0

Method: FOUR score

- Data for the calculation of this score were considered valid only when determined in the absence of sedatives or paralytics and within 6 h after arrest
- NE were completed by one of the authors for 222/457 (49%) of subjects. The remainder was obtained from either the critical care attending note or the ICU nursing note

Method

- SOFA and FOUR scores were calculated prior to arrival at goal temperature
- Only cases lacking these data, or for which specific data were not recorded until more than 6 h after ROSC, were considered inadequate and excluded

Method: outcome measures

- Survival to hospital discharge
  - Good NE outcome : discharged to home or acute rehabilitation
  - Poor NE outcome: discharged to a skilled nursing facility, long-term acute care facility, or death
- Neurological status at death or hospital discharge
- Development of MOF

Method: outcome measures

- "Good" status corresponds to cerebral performance categories (CPC) 1 or 2
- "Poor" status corresponds to CPC 3–4
- **Cerebral performance category scale**

Cerebral performance category scale
CPC 1
    A return to normal cerebral function and normal living
CPC 2
    Cerebral disbility but sufficient function for independent activities of daily living
CPC 3
    Severe disability, limited cognition, inability to carry out independent existence
CPC 4
    Coma
CPC 5
    Brain death

Method: Statistical analysis

- Single-variable logistic regression was completed on each SOFA and FOUR subscore as well as age, gender, primary rhythm of arrest, location of arrest (IHCA or OHCA), treatment with TH, initial temperature, and year of treatment to determine if it was associated with survival, MOF, or good outcome

Method: Statistical analysis

- **The Chi-Square automatic interaction detector (CHAID)**
  - used to analyze interactions between candidate predictor variables from the single-variable logistic regression and three outcome measures: survival, good outcome, and MOF

Method: Statistical analysis

	Survival OR (95% CI)	Good Outcome OR (95% CI)	MOF OR (95% CI)
FOUR			
Motor	2.21 (1.91, 2.56)	2.01 (1.72, 2.35)	0.62 (0.53, 0.73)
Brainstem	2.41 (2.02, 2.87)	2.16 (1.76, 2.64)	0.62 (0.54, 0.72)
Respiratory	1.55 (1.31, 1.84)	1.47 (1.25, 1.73)	0.73 (0.59, 0.89)
Eye	1.61 (1.40, 1.85)	1.51 (1.32, 1.73)	0.69 (0.58, 0.82)
SOFA			
Cardiac	0.73 (0.64, 0.84)	0.73 (0.63, 0.86)	1.49 (1.29, 1.71)
Respiratory	0.81 (0.69, 0.96)	0.89 (0.75, 1.07)	1.54 (1.27, 1.87)
Renal	0.64 (0.50, 0.82)	0.62 (0.47, 0.82)	1.67 (1.32, 2.11)
Liver	0.89 (0.60, 1.32)	1.04 (0.70, 1.57)	1.38 (0.93, 2.05)
Coagulation	0.79 (0.55, 1.13)	0.89 (0.61, 1.31)	1.89 (1.31, 2.74)

Method: Statistical analysis

- FOUR Motor and FOUR Brainstem were most consistently associated with **survival** and **good outcome** in both univariable and multi-variable regression
- SOFA Cardiovascular and SOFA Respiratory were associated with **survival** and **MOF**

Method: Statistical analysis

- Neurologic variable
  - **FOUR Motor-Brainstem**
  = FOUR Motor + FOUR Brainstem
- Organ failure variable
  - **SOFA Cardiac-Respiratory**
  = SOFA Cardiac + SOFA Respiratory

Results

- 495 subjects treated during this time period, 457 had valid data for analysis
- Excluded subjects (N = 38) more frequently experienced IHCA, were comatose, and loss of data during the change in electronic medical record systems for the ICU

Results: Regression analysis

	Survival OR (95% CI)	Good Outcome OR (95% CI)	MOF OR (95% CI)
FOUR			
Motor	2.21 (1.91, 2.56)	2.01 (1.72, 2.35)	0.62 (0.53, 0.73)
Brainstem	2.41 (2.02, 2.87)	2.16 (1.76, 2.64)	0.62 (0.54, 0.72)
Respiratory	1.55 (1.31, 1.84)	1.47 (1.25, 1.73)	0.73 (0.59, 0.89)
Eye	1.61 (1.40, 1.85)	1.51 (1.32, 1.73)	0.69 (0.58, 0.82)
SOFA			
Cardiac	0.73 (0.64, 0.84)	0.73 (0.63, 0.86)	1.49 (1.29, 1.71)
Respiratory	0.81 (0.69, 0.96)	0.89 (0.73, 1.07)	1.54 (1.27, 1.87)
Renal	0.64 (0.50, 0.82)	0.62 (0.47, 0.82)	1.67 (1.32, 2.11)
Liver	0.89 (0.60, 1.32)	1.04 (0.70, 1.57)	1.38 (0.93, 2.05)
Coagulation	0.79 (0.55, 1.13)	0.89 (0.61, 1.31)	1.89 (1.31, 2.74)
Age	1.0 (0.99, 1.01)	0.98 (0.97, 0.99)	0.99 (0.98, 1.01)
Male sex	1.12 (0.78, 1.63)	1.48 (0.99, 2.22)	0.88 (0.56, 1.38)
OHCA	0.84 (0.58, 1.22)	1.24 (0.83, 1.85)	1.82 (1.14, 2.92)
Initial Rhythm			
VF/VT	2.92 (1.98, 4.29)	3.50 (2.31, 5.28)	0.68 (0.42, 1.09)
PEA	0.52 (0.34, 0.78)	0.52 (0.33, 0.84)	1.10 (0.67, 1.80)
Asystole	0.56 (0.34, 0.91)	0.35 (0.19, 0.64)	1.55 (0.91, 2.64)
Unknown	0.75 (0.42, 1.35)	0.70 (0.36, 1.35)	1.01 (0.48, 2.05)
Hypothermia Received	0.32 (0.22, 0.47)	0.33 (0.21, 0.50)	3.05 (1.90, 4.89)
Year of Treatment	0.99 (0.87, 1.13)	0.89 (0.78, 1.03)	1.16 (0.99, 1.37)
Temp at hospital arrival (°C)	1.06 (0.94, 1.20)	1.07 (0.94, 1.22)	0.80 (0.69, 0.92)

Results: Regression analysis

- Good outcome was associated
  - FOUR Motor (OR 1.70; 95% CI 1.35, 2.14)
  - FOUR Brainstem (OR 1.71; 95% CI 1.30, 2.24)
  - Age (OR 0.97; 95% CI 0.95, 0.99)
  - Primary rhythm of VF/VT (OR 2.60; 95% CI 1.48, 4.59)

Results: Regression analysis

- MOF was associated
  - FOUR Brainstem (OR 0.70; 95% CI 0.58, 0.85)
  - SOFA Cardiovascular (1.69; 95% CI 1.36, 2.10)
  - SOFA Respiratory (OR 1.48; 95% CI 1.15, 1.92)
  - SOFA Renal (OR 1.54; 95% CI 1.12)
  - SOFA Coagulation (OR 1.76; 95% CI 1.08, 2.86)

Results: Regression analysis

- FOUR Motor-Brainstem had a univariable association with
  - Survival (OR 1.71; 95% CI 1.55, 1.88)
  - Good outcome (OR 1.60; 95% CI 1.44~1.77)
  - MOF (OR 0.76; 95% CI 0.70, 0.82)

Results: Regression analysis

- SOFA Cardiac-Respiratory had a univariable association with
  - Survival (OR 0.78; 95% CI 0.71, 0.84)
  - Good outcome (OR 0.80; 95% CI 0.73, 0.88)
  - MOF (OR 1.51; 95% CI 1.37, 1.67).

Results: CHAID analysis

- FOUR Brainstem was the primary predictor of survival (Chi-Square 138.074, p < 0.001)
- Good outcome was primarily predicted by FOUR Motor (Chi-Square 95.66, p < 0.001)

Results: CHAID analysis

- Combination variable of FOUR Motor-Brainstem that provided optimal categorization of the population for both survival (Chi-Square 172.47, p < 0.001) and good outcome (Chi-Square 110.33, p < 0.001)
- SOFA Cardiac-Respiratory ≥4 was most predictive of development of MOF (Chi-Square 77.81, p < 0.001).

Results: CHAID analysis

- Grouping subjects according to neurological score (FOUR Motor-Brainstem 0–3, 4–7, 8) and cardiopulmonary dysfunction (SOFA Cardiac-Respiratory 0–3, 4–8) initially yielded six different categories of illness severity

## Results: CHAID analysis
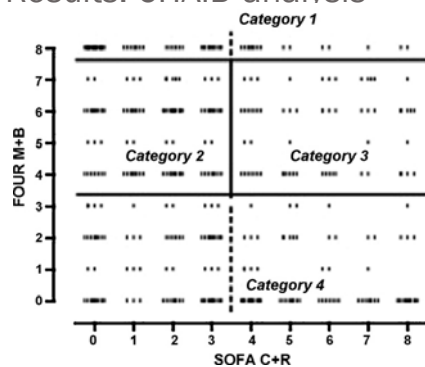
Results: CHAID analysis

- Subjects in the FOUR Motor-Brainstem < 4 and in the FOUR Motor-Brainstem > 7 groups experienced similar outcomes throughout the range of SOFA Cardiac-Respiratory scores
- These were combined for simplification, resulting in four categories with the following descriptions

Results: CHAID analysis

- Categories of post-cardiac arrest early illness severity
  - Category I: **Awake**
  - Category II: **Moderate coma without cardiorespiratory failure**
  - Category III: **Moderate coma with cardiorespiratory failure**
  - Category IV: **Severe coma**

Results: Outcome
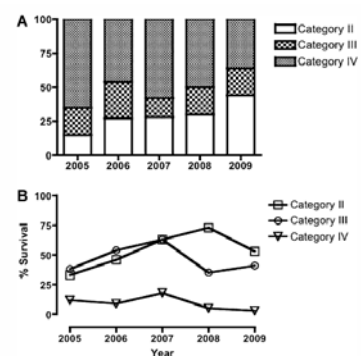
Results: Outcome

- An initial rhythm of VF/VT was less common in category IV subjects

Table 2
Post cardiac arrest category, patient characteristics, treatments, and outcome. Therapeutic hypothermia achieved delineates the group where temperature ≤34°C was achieved.

	Category I (N = 141)	Category II (N = 98)	Category III (N = 63)	Category IV (N = 155)
Age, in years (SD)	62 (15)	61 (15)	62 (16)	60 (19)
Male sex	88 (62%)	49 (50%)	41 (65%)	81 (52%)
OHCA[a]	52 (37%)	68 (69%)	24 (38%)	109 (70%)
Rhythm[b]				
VF/VT	69 (49%)	49 (50%)	27 (43%)	40 (26%)
PEA	35 (25%)	24 (25%)	16 (25%)	56 (36%)
Asystole	23 (16%)	10 (10%)	14 (22%)	42 (26%)
Unknown	13 (10%)	15 (15%)	6 (10%)	18 (12%)
	Category I (N = 106)	Category II (N = 71)	Category III (N = 48)	Category IV (N = 119)
Temperature during initial clinical examination (°C) (SD)[a,b]	35.9 (1.5)	35.5 (1.5)	35.4 (2.3)	35.1 (1.9)
Therapeutic hypothermia intended[b]	8 (6%)	76 (78%)	33 (52%)	104 (67%)
Therapeutic hypothermia achieved[b]	4 (3%)	71 (72%)	29 (46%)	98 (63%)
Coronary angiography[b]	65 (56%)	43 (64%)	15 (31%)	37 (30%)
Death from poor neurologic prognosis	5 (4%)	29 (30%)	16 (25%)	66 (43%)

a Initial temperature not available for all subjects.
b p < 0.01 between groups.

Results: Outcome

- OHCA was more common in category II and IV subjects

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Results: Outcome

- Temperature at initial examination was lowest in category IV subjects

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Results: Outcome

- TH was rarely applied to category I subjects

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b p < 0.01 between groups.

Results: Outcome

- Coronary angiography was less commonly performed for category III and IV subjects

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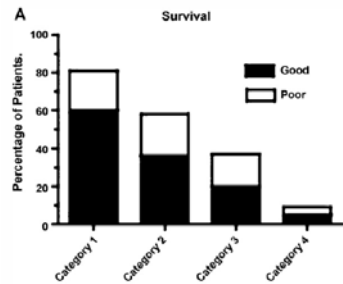

Results: Outcome

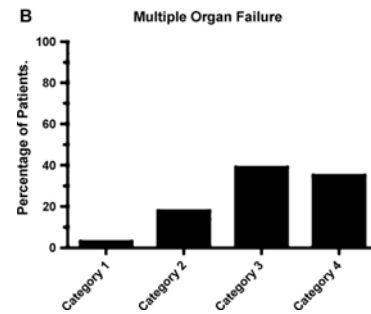- Survival was independently associated with category as was OHCA
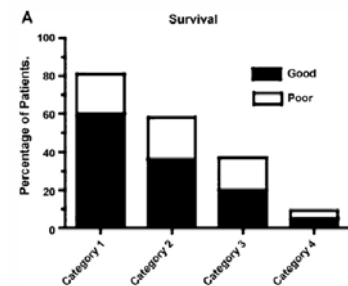
Results: Outcome

- Likewise, Good outcome was associated with category age and OHCA

Results: Outcome

- Development of MOF was associated with category along

Discussion

- The category of early illness severity had a stronger association with survival, good outcome and cause of death

Discussion

- Physiological state of the patient after ROSC appears to be highly associated with the subsequent clinical course
  - Initial examination and laboratory results available in the first 6 h following ROSC may be used to provide immediate prognostic information to families and clinicians

Discussion

- Previously noted that patients in deep coma were less likely to receive coronary angiography
- 4 patients with ST elevation myocardial infarction did not receive this therapy due to poor neurologic status
- **No category of initial illness severity excludes good neurologic outcome**
- These data **do not support withholding aggressive post arrest care** for comatose patients

Discussion

- The categories of early illness severity derived in this paper explain a variety of observations about post-cardiac arrest patients
  - Category III is largely comprised of IHCA cohort and is the category most likely to suffer from MOF
  - IHCA has previously been reported to have a higher rate of progression to MOF compared to OHCA

Discussion

- Cardiac arrest with an initial rhythm of VF also is more likely than non-VF rhythm to result in category I or II patients, with excellent prognoses, versus category IV patients, with poor prognoses

Table 2
Post cardiac arrest category, patient characteristics, treatments, and outcome. Therapeutic hypothermia achieved delineates the group where temperature ≤34 °C was achieved.

	Category I (N = 141)	Category II (N = 98)	Category III (N = 63)	Category IV (N = 155)
Age, in years (SD)	62 (15)	61 (15)	62 (16)	60 (19)
Male sex	88 (62%)	49 (50%)	41 (65%)	81 (52%)
OHCA	52 (37%)	68 (69%)	24 (38%)	109 (70%)
Rhythm				
VF/VT	69 (49%) ←	49 (50%) ←	27 (43%)	40 (26%)
PEA	35 (25%)	24 (25%)	16 (25%)	56 (36%)
Asystole	23 (16%)	10 (10%)	14 (22%)	42 (26%)
Unknown	13 (10%)	15 (15%)	6 (10%)	18 (12%)
	Category I (N = 106)	Category II (N = 71)	Category III (N = 48)	Category IV (N = 119)
Temperature during initial clinical examination (°C) (SD)	35.9 (1.5)	35.5 (1.5)	35.4 (2.3)	35.1 (1.9)
Therapeutic hypothermia intended	8 (6%)	76 (78%)	33 (52%)	104 (67%)
Therapeutic hypothermia achieved	4 (3%)	71 (72%)	29 (46%)	98 (63%)

Discussion

- Category can be used to counsel about prognosis, selecting patients for clinical trials, and comparing populations between different clinical trials or settings
- Early illness severity explains much of the variation in outcome between IHCA and OHCA and between VF and non-VF cardiac arrest

Discussion

- There are several limitations to this study
  - Subjects with greater illness severity had lower initial core temperatures on hospital arrival
  - This may represent an inability to maintain core temperature in subjects with most severe neurologic injury
  - may have confounded the initial neurologic examination

Discussion

- Some subjects did receive prehospital cooling,
- This is unlikely to have affected outcome as a recent clinical trial demonstrated no change in outcome with prehospital cooling
- It is also possible that the initial neurologic examination was less regimented prior to
- implementation of TH and a post-cardiac arrest care plan
- Restricted this analysis to patients without sedation and with well-documented examinations by attending physicians

Conclusion

- Initial illness severity explains much of the variation in cardiac arrest outcomes.
- This model provides prognostic information at hospital arrival and a universal nomenclature to stratify patients in future studies

Thank you for your attention!!