Prognostic values of blood ammonia and partial pressure of ammonia on hospital arrival in out-of-hospital cardiac arrests

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Introduction

- Outcome prediction of OHCA is important
- Lack of prognostic predictor of ROSC
  (Glasgow Coma Score , brain stem reflex , somatosensory-evoked potentials , end-tidal carbon dioxide , S-100 protein , neuron-specific enolase, serum glucose , serum lactate , and brain natriuretic peptide)
- Hepatic dysfunction: common in critically ill patients
  - spontaneous hypoglycemia, respiratory insufficiency, and hyperammonemia
- We hypothesized that **blood ammonia** levels may reflect **tissue hypoxia**

→used to predict the likelihood of ROSC achievement for OHCA patients.

Introduction

- Ammonia
  - Ammonium (NH_4^+) in blood (most)
  - pNH3 (<2%, non-ionized form, pH-dependent, permeates cell membranes, more toxic)
- Acidosis is one of the cause of cardiac arrest (pH↓ affects pNH3)

➔pHN3 should be a predictive tool for ROSC

Materials and methods-Study setting

- prospective, observational study
- tertiary university hospital in Taiwan between 2008.01 and 2008.12
- consecutive OHCA patients sent to the ED
- Exclusion: pregnancy, severe hypothermia, DNR, irreversible death, younger than 18 years old
- The data by Utstein-style criteria
  (patient's history, cardiac risk factors, response intervals, initial cardiac rhythms, and the extent and amount of emergency care.)
- BLS and ASLS based on 2005 AHA guideline

Assessment of the blood ammonia levels and the pNH3

- **femoral vessels**, within 5 minutes
- **Ammonia levels** were measured by Vitros Fusion 5.1 FS Automated Chemistry Analyzer (range:1~500μmol/L)
- The **blood gas analysis** was determined using i-STAT EG7+ cartridges with i-STAT System
  - The patients who did not follow the aforementioned blood sampling procedures were excluded.

Outcome measures

- primary outcome was **ROSC**

Statistical analysis

- Data were collected by the designated registered nurses
- The ROSC and the non-ROSC group:compared
  - by **Mann-Whitney U test** for continuous variables
  - by **χ2 test or Fisher test** for discrete variables
- The sensitivity and specificity of the prediction of non-ROSC: calculated for different cutoff values of blood ammonia levels and the pNH3,
  - Results: depicted as a receiver operating characteristics (ROC) curve with an area under the curve (AUC).

Results

- 175 OHCA
  - 4<18 y/o,
  - 12 irreversible death,
  - 12 hypothermia,
  - 16 DNR,
  - 14 no blood sampling,
  - 8 unavailable lab data

→119 p't

Table 1 Clinical and biochemical parameters among patients with OHCA

	Total OHCA	Non-ROSC group	ROSC group	*P*
Total	119	91	28	
Age (y)	74 (61.0-80.5)	74.0 (59.0-81.0)	73.5 (63.5-79.0)	.856
Sex (male)	60 (50.4%)	47 (51.6%)	13 (46.4%)	.927
Etiology (nontrauma)	94 (79.0%)	70 (76.9%)	24 (85.7%)	<.05
Witness cardiac arrest	49 (41.1%)	33 (36.3%)	16 (57.1%)	.054
Bystander CPR	10 (8.4%)	8 (8.79%)	2 (7.14%)	<.05
Initial cardiac rhythm (shockable)	28 (23.5%)	18 (15.1%)	10 (35.7%)	<.05
Ammonia (μmol/L)	150.0 (108.0-187.5)	167.0 (120.0-190.0)	80.0 (47.5-96.0)	<.05
pNH3 (10^{-5} mm Hg)	2.38 (1.67-3.47)	2.61 (1.88-3.81)	1.67 (0.89-2.31)	<.05
White blood counts (10^{-3}/μL)	10.7 (7.8-14.2)	10.5 (7.6-13.8)	11.7 (8.8-17.2)	.319
Hemoglobin level (g/dL)	11.3 (8.6-13.6)	11.2 (8.6-13.4)	11.5 (8.5-14.7)	.694
AST (U/L)	81 (42.5-208.0)	84 (44.0-270.5)	52 (34.5-111.0)	.06
ALT (U/L)	39 (19-131.5)	42 (21.5-151.0)	24 (15.0-63.0)	<.05
Creatinine (mg/dL)	1.7 (1.1-2.6)	1.6 (1.1-2.3)	2.4 (1.4-4.2)	<.05
Sodium (mmol/L)	141.0 (137.0-144.0)	142.0 (138.0-145.0)	140.5 (134.5-142.5)	.110
Potassium (mmol/L)	5.6 (4.6-7.3)	5.8 (4.6-7.5)	4.9 (4.3-6.2)	<.05
Glucose (mg/dL)	148.0 (89.5-231.5)	142.0 (82.0-212.0)	165.0 (118.0-202.0)	.497
pH	7.0 (6.9-7.2)	7.0 (6.8-7.2)	7.1 (7.0-7.2)	<.05
P_{O_2} (mm Hg)	20.0 (13.0-38.7)	20.0 (12.0-37.0)	21.9 (14.5-71.0)	.145
P_{CO_2} (mm Hg)	67.7(49.2-89.7)	71.6(55.0-100.0)	55.3(44.0-69.9)	<.05
Bicarbonate (mmol/L)	19.5 (12.7-23.9)	20 (13.1-24.3)	18.6 (12.4-21.5)	.34
BE (mmol/L)	−10 (−19.0 to −6.0)	−9.7 (−19.5 to −6.0)	−12 (−17 to −5.6)	.86

Categorical variables were given as number (percentage), whereas quantitative data were given as median (interquartile range). *P* value comparing non-ROSC achievement group and ROSC achievement group less than .05 was considered significant. AST indicates aspartate aminotransferase; ALT, alanine aminotransferase; BE, base excess.

Ammonia levels and pNH3 values at ED arrival

- blood gas and ammonia levels obtained within **2 and 15** minutes
- The median ammonia level: 150 μmol/L (IQR, 108-187.5 μmol/L).
- 115 patients (96.6%) > upper institutional normal limit of 33 μmol/L

Ammonia levels and pNH3 values at ED arrival

- Ammonia levels and pNH3 values in the non-ROSC group were significantly higher than the levels in the ROSC achievement group (P<0 .05)

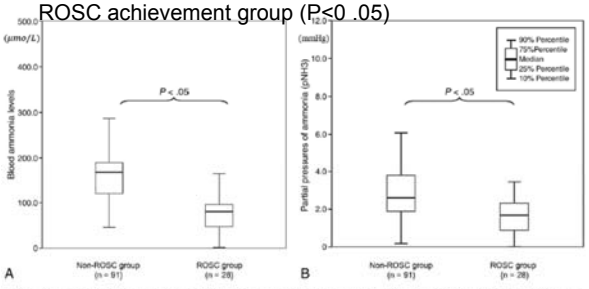
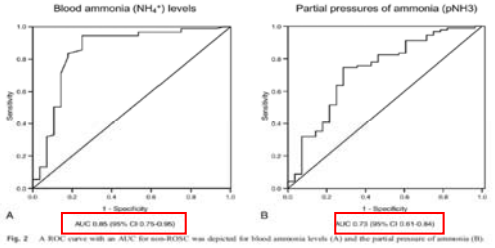


Fig. 1 Comparison of blood ammonia levels (A) and the partial pressures of ammonia (B) of the non-ROSC group and the ROSC group.

The prognostic value of ammonia levels and pHN3

1. The optimal cutoff level: 84 μmol/L 2. Se: 94.5%, Sp:75% for predicting non-ROSC with a diagnostic accuracy of 89.9%.
3. The pretest odds ratio was 3.2, and the posttest odds ratio was 12.3.

1. The optimal cutoff pNH3 value of 1.89 × 10−5 mm Hg
2. Se: 74.7%, Sp:71.4% for predicting non-ROSC with a diagnostic accuracy of 73.9%.
3. The posttestodds ratio was 8.5.



Comparison of the non-ROSC and the ROSC achievement group

Table 2 Clinical and biochemical variables significantly influencing achievement of ROSC were dichotomized using discriminant values derived by constructing ROC curves for each variable

	Non-ROSC group (n = 91)	ROSC group (n = 28)	*P*	Odds ratio (95% CI)
Etiology			.32	3.2 (1.0-10.3)
Nontrauma	70 (76.9%)	24 (85.7%)		
Trauma	21 (23.1%)	4 (14.3%)		
Bystander CPR			.78	1.3 (0.3-6.3)
Absent	83 (91.2%)	26 (92.6%)		
Present	8 (8.8%)	2 (7.4%)		
Initial cardiac rhythm			.08	0.4 (0.2-1.1)
Nonshockable	73 (80.2%)	18 (64.3%)		
Shockable	18 (19.8%)	10 (35.7%)		
Ammonia (μmol/L)			<.05	51.6 (14.9-178.8)
<84.0	5 (5.5%)	21 (75.0%)		
≥84.0	86 (94.5%)	7 (25.0%)		
pNH$_3$ (10^{-5} mm Hg)			<.05	7.4 (2.9-19.0)
<1.89	23 (25.3%)	20 (71.4%)		
≥1.89	68 (74.7%)	8 (28.6%)		
ALT (U/L)			<.05	3.1 (1.3-7.6)
<36.5	37 (40.7%)	19 (67.9%)		
≥36.5	54 (59.3%)	9 (32.1%)		
Creatinine (mg/dL)			.61	1.4 (0.3-6.0)
<0.85	7 (7.7%)	3 (10.7%)		
≥0.85	84 (92.3%)	25 (89.3%)		
Potassium (mmol/L)			<.05	2.9 (1.2-7.2)
<5.5	38 (42.8%)	19 (67.9%)		
≥5.5	53 (58.2%)	9 (32.1%)		
pH			.33	N/A
<7.36	88 (96.7%)	28 (100%)		
≥7.36	3 (3.3%)	0 (0%)		
PCO$_2$ (mm Hg)			<.05	11.6 (2.6-52.0)
<78.4	48 (52.7%)	26 (92.9%)		
≥78.4	43 (47.3%)	2 (7.1%)		

Odds ratio with 95% CI for each variable was listed. N/A indicates not applicable.

Discussion

- Ammonia level **cutoff** value
  - Nagamine: <105.6μmol/L→predictive for full neurologic recovery in witnessed OHCA patients
  - Yanagawa:ammonia levels were significantly higher among the survivors with higher cerebral performance category (CPC) scores 1 month after cardiac arrest
  - Shinozaki: ammonia level >99.8μmol/L→independent predictor of higher CPC scores 6 months of cardiac arrest
- Ammonia↑➔ nonionize form↑ ➔blood pH↑➔a great of ammonia enter into brain
  - Bhatia: arterial ammonia level>124μmol/L: predictor of mortality in p't with acute hepatic failure(no difference between blood ammonia and pHN3)
  - Our study: blood ammonia is superior than pHN3
- Tissue hypoxia➔ammonia ↑
  - Nagamine:blood ammonia level of OHCA positively correlated with the time elapsed from confirmation of cardiac arrest to hospital arrival
  - Ishida: respiratory and metabolic acidosis during cardiac arrest→ ammonia ↑ from RBC

  ➔➔cardiac arrest→tissue hypoxia→ammonia production→can be a predictor of non-ROSC of OHCA p't

Discussion

- ↓elimination of ammonia (liver and kidney)➔ ammonia ↑
- Pathogenesis: hyperammonemia →
  - impaired bioenergetics,
  - altered neurotransmission,
  - glutamate-mediated excitotoxicity, electrophysiologic derangements, oxidative and nitrosative stress,
  - mitochondrial dysfunction
- mainly toxic to the brain, complications is neurologic

Discussion

- We found that hyperammonemia was **independently predictive** of non-ROSC in OHCA patients.
- Physicians should consider terminating resuscitation efforts for OHCA patients if the initial ammonia levels are extremely high.

limitation

- arterial or venous?
- the time between arrest and laboratory sampling was unknown
- laboratory reports of biomarkers in this study was not blinded.

conclusion

- A blood ammonia level > 84μmol/L : Se 94.5% and Sp 75.0% for predicting non-ROSC in OHCA patients with a diagnostic accuracy of 89.9%.
- The predictive value of the blood ammonia level for non-ROSC is better than that of the pNH3.

Minor head injury in the elderly at very low risk: a retrospective study of 6 years in an Emergency Department (ED)

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Introduction

- Mild head injury (MHI): common in accident and ED, but management is not homogeneous
- Numerous guidelines focus on
  - period of observation of the patients
  - right time for discharge,
  - Assessment
  - specialized equipment needed
- Particular attention: **who needs CT scan?**
  - Italian guidelines on MHI: GCS 14 to 15 and no neurological deficits or open injuries.
  - pre-existing risk factors and factors subsequent to trauma

Introduction

- Long-standing debate about MHI in the elderly
  - current guidelines recommend routinely performing a CT(>60 or >65 y/o)
  - Many author think **age is an independent risk factor**
- According to Italian guidelines: >65y/o with low risk MHI→ CT scan and short-term observation

➔high number of recorded CT scans: negative

➔need for a retrospective study investigating this group of patients and use of CT.

Materials and methods

- retrospective study
- patients older than 65
- between April 2004 and April 2010.

Table 1 Inclusion and Exclusion Criteria for our study

Inclusion criteria	Exclusion criteria
GCS 15	GCS < 15
Clear dynamics of trauma with exclusion of dangerous events (see Exclusion Criteria)	Dangerous events: falls from height above 1 meter; car, motorcycle or bicycle accidents; pedestrian vs. vehicle collision;
No or minor wounds	Deep wounds or sign of skull fractures
Absence of neurological defects, or history of neurological disease or previous neurosurgical intervention	Presence of neurological defects (also related to previous neurological disorders); history of neurological disorders (also seizures), previous neurological intervention
No history of coagulation disorders, and no assumption of oral anticoagulants	Consumption of oral anticoagulant, history of coagulopathy
No symptoms after head injury (except pain in site of injury)	Symptoms related to injury, ie, diffuse headache, vomiting, loss of consciousness after MHI, diplopia, amnesia Assumption of alcohol or illicit drugs

Materials and methods

- primary outcome: any intracranial traumatic findings on CT
- secondary outcome: possible neurosurgical intervention subsequent to CT scan results

Result

- 4518 >65y/o (range, 65–107 years)

Table 2 Distribution of excluded patients

Patients excluded	2369
Major or moderate head injury	40
Presence of alterations at neurological examination	255
Abnormal conscious state for dementia or psychosis	525
Symptoms (ie, diffuse headache, vomiting, diplopia, amnesia, loss of consciousness); deep wounds or dangerous dynamics	290
History of coagulopathy, oral anticoagulant assumption, previous neurosurgical intervention, neurological disorder, alcohol or illicit drugs assumption	1259

- mean age:81y/o (95% CI 80.96-81.62, SD 7.728)
- 959 men and 1190 women
- The time of presentation after injury was between 30 minutes and 72 hours.

Result

Table 3 Primary and secondary outcome of included patients

Acute findings on CT	Patients underwent neurosurgery	Patients without neurosurgical treatment
Subarachnoid hemorrhage	1	20
Subdural hematoma	2	13
Cerebral contusions	-	9
Parenchymal bleeds	-	2

Table 4 Distribution of included patient in different age groups

Year group	Patients	Acute findings on CT
65-69 years	180	0 (0%)
70-74 years	301	2 (0.6%)
75-79 years	435	4 (0.9%)
80-84 years	539	18 (3.3%)
85-89 years	387	14 (3.6%)
90-94 years	225	7 (3.1%)
>95 years	82	2 (2.4%)
Total	2149	47 (2.18%)

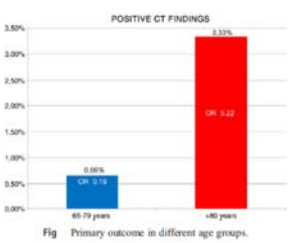

Fig Primary outcome in different age groups.

result

Table 5 Primary outcome in population on antiplatelet treatment

Age	Patients (n)	Intracranial bleedings (n)	%	Median age	SD	95% CI
65-69.99	36	0	0	68.03	1.33	67.6-68.46
70-74.99	66	0	0	72.67	1.33	72.35-72.99
75-79.99	130	3	2.3	77.84	1.47	77.59-78.09
80-84.99	173	10	5.78	82.63	1.46	82.41-82.85
85-89.99	138	4	2.89	87.20	1.46	86.96-87.44
90-94.99	57	4	7.02	91.81	1.42	91.44-92.18
>95	17	1	5.88	96.37	1.4	95.7-97.04

Table 6 Statistical analysis of primary outcome of population on antiplatelet treatment

Age	OR	95% CI	P
65-69.99	–	–	–
70-74.99	–	–	–
75-79.99	7.13	0.74- 69.70	.09
80-84.99	3.15	1.06-7.08	< .005
85-89.99	0.71	0.22-2.32	.568
90-94.99	4.1	0.90-19.14	.0516
>95	4.06	0.23-67.48	.3

- 617 on antiplatelet: 22 (3.72%) had an acute pathological finding on CT scan.
  - 1532 without antiplatelet: 25 (1.63% OR: 2.23) had an acute pathological finding on CT scan
- The rate of pathological findings on CT:
  - 3.31% **acetylsalicylic acid** (OR 2.01, 95% CI 1.07- 3.74, P b .005),
  - 5.6% among patients with **ticlopidine** (OR 3.60, 95% CI 1.22-10.63, P = .0134),
  - 12,5% in patients with **doubled antiplatelet therapy** (clopidogrel plus acetylsalicylic acid , OR 5.67, 95% CI 1.02-72.7, P = .0173).

Result

- 634 p't with scalp wound: 19(3.14%) CT finding
  - 1515 without wound: 2.19% (odds ratio 1.64, 95%CI 0.91-2.96, P = 0.1).
- 303 p't with HTN under anti-PLT :7 (3.06%) CT finding
  - 1199 without HTN without anti-PLT: 14(1.17%, Odds Ratio 2.00, 95% CI 1.12-3.64 P = .17)
- No correlation between the **time of presentation** at the ED after head injury
  - the mean time: 5hr
  - 983 within 3 hours: 24 acute findings on CT(OR 1.24, 95% CI 0.70-2.22, P = ,46)
  - 1166 patients after 3hours(<72hrs): 23 acute findings on CT (OR 0.80, 95% CI 0.45-1.43 P = .46).

Discussion

- Italian guideline: > 65 y/o MHI without risk factors should undergo CT
- Generalizability of New Orleans Criteria and Canadian CT Head Rules is limited with no risk factors except age
  - Italian guideline: 1-3% p't with MHI develop intracranial complication
- Based on our retrospective analysis of elderly p't at very low risk→ seem to not necessary (2.18% CT finding)

➔advance age only no longer seems to be important (at least when age<80 y/o)

- P't >80 y/o, significant increase rate of complications

Discussion

- anticoagulants is a significant risk factor for spontaneous and traumatic intracranial haemorrhage in old patient >65 y/o

➔CT is recommended

Conclusion

- MHI without risk factor age between 65-79

→ don't need CT scan

- MHI with very old p't (> 80y/o) and anti-PLT Tx

→need CT scan

- Thanks for your attention ! !