Journal Reading

Reporter: 輔大Int 陳詩宇
Supervisor: 王瑞芳醫師
101.11.19

Hyperfibrinolysis in out of hospital cardiac arrest is associated with markers of hypoperfusion

V.A. Viersen et al., Resuscitation 83 (2012) 1451– 1455

Background

- Cardiopulmonary arrest VS Hyperfibrinolysis
- Severity of hyperfibrinolysis associated with the degree of shock and hypoperfusion?

Material and Method

- Inclusion criteria
  - Age≧18 y/o
  - Witness out of hospital cardiac arrest but not related to trauma

Material and Method

- Exclusion criteria
  - Inability to drawn blood samples
  - Previous haemostatic abnormalities
  - Traumatic arrest
  - Pregnancy
  - Cardiac arrest from septic shock
  - Use of heparin or warfarins
  - Suspected (massive) pulmonary embolism

Material and Method

- Hyperfibrinolysis
  - Definition: maximum lysis of the clot of >20% within 60 min following initiation of rotational thromboelastometry in the EXTEM channel
- Maximum lysis index (ML): Max MCF-Min MCF (%)
- Lysis onset time (LOT): Rx=>lysis of 20%

Table 1
Characteristics of patients without or with hyperfibrinolysis.

	No hyperfibrinolysis	Hyperfibrinolysis	*P*
N	14	16	
Age (years)	65 ± 18	68 ± 13	ns
Resuscitation parameters			
Median transportation time (min)	44 (34–49)	38 (32–53)	ns
Median CPR time (min)	10 (7–18)	36 (15–55)	0.001
Median time to 1st output (min)	16 (13–28)	44 (33–58)	0.007
Coagulation parameters			
Haemoglobin (mmol/l)	8.3 ± 1.0	8.5 ± 1.2	ns
Haematocrit	0.41 ± 0.05	0.43 ± 0.06	ns
aPTT (s)	38 ± 10	54 ± 16	0.006
INR	[illegible]	[illegible]	ns
Platelet count (10^{-9})*	[illegible]	[illegible]	ns
Fibrinogen (g/l)	[illegible]	[illegible]	ns
D-dimers (μg/ml)	2.3 ± 2.0	6.1 ± 2.1	0.02
Markers for hypoperfusion			
pH	7.17 ± 0.15	6.96 ± 0.11	<0.001
BE	−11.91 ± 6.44	−20.01 ± 3.53	<0.001
Lactate (mmol/l)	8.0 ± 3.7	13.1 ± 3.7	0.001
Median pO_2 (kPa)	237 (127–405)	92 (54–124)	0.001
Median pCO_2 (kPa)	44 (35–52)	59 (46–78)	0.03

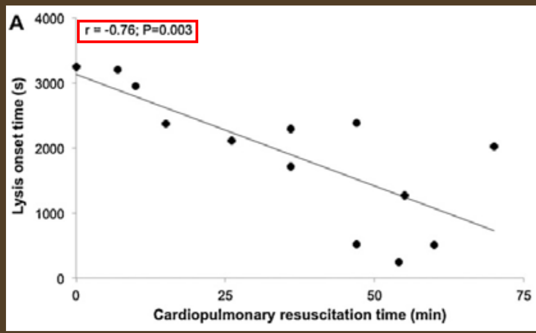
Hyperfibrinolysis associated with signs of DIC

Values are presented as mean ± SD or median with interquartile range. CPR, cardiopulmonary resuscitation; aPTT, activated partial thromboplastin time; INR, international norm[...]

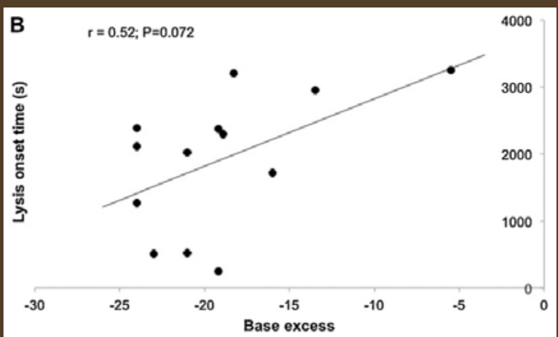
Hyperfibrinolysis associated with markers of hypoperfusion

* P < 0.05 was considered as statistically different.

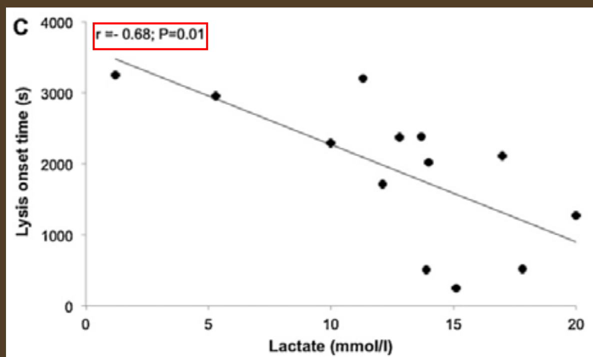
Result



Result



Result



Result

- Lysis onset time correlates well with CPR time and lactate levels
- Lactate associated with the maximum lysis (r = 0.52; P = 0.04), LI30 (r =−0.61; P = 0.01) and LI45 (r = −0.87; P < 0.001)

Discussion

- A significant part of OHCA patients develop hyperfibrinolysis, in particular in case of signs of hypoperfusion => hyperfibrinolysis may be induced by shock and hypoperfusion solely, without the presence of trauma or massive blood loss

Disucssion

- Degree of hyperfibrinolysis: how to determine?
- Body temperature, a confounding factor?
- Hyperfibrinolysis vs mortality and morbidity

Etomidate is associated with mortality and adrenal insufficiency in sepsis: A meta-analysis

Chee Man Chan et al, Crit Care Med 2012 Vol. 40, No. 11

Background

- To evaluate the effects of single-dose etomidate on the adrenal axis and mortality in patients with severe sepsis and septic shock

Material and Method

- Meta-analysis of RCT and observational studies
- January 1950 and February 2012: EMBASE, Medline, Cochrane Database

Material and Methods

- Inclusion criteria (for mortality)
  - randomized or prospective observational approach
  - control group
  - provided sufficient quantitative data to evaluate mortality (either in–hospital or 28-day)

Material and Method

- Inclusion criteria (for adrenal insufficiency)
  - Presence of AI (formal cosyntropin stimulation test or measurement of random cortisol level with a value ≤15 μg/dL)
  - Control group
  - Quantitative data
  - Retrospective or prospective

Result

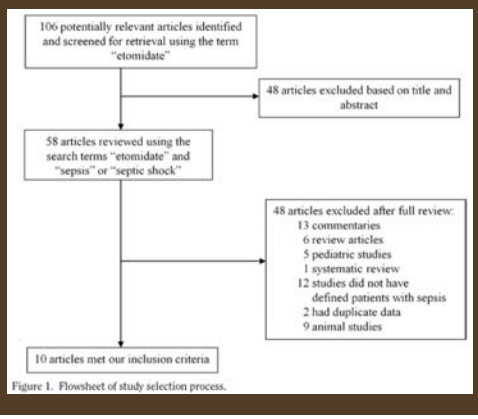


Figure 1. Flowsheet of study selection process.

Results

- Mortality
- Adrenal insufficiency

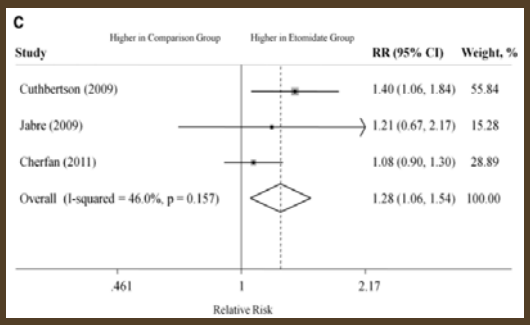
} VS Etomidate

Mortality

Table 1. Studies included for mortality

Study/Year (Country-Language)	Intervention	Design	Age, yrs[a]	Patients, n	Male Gender, %	Severity of Illness, (Score)[a]	End Point	Mortality in Etomidate Group, n (%)	Mortality in Comparison Group, n (%)	Quality Score	Quality Problems
Cuthbertson et al/2009 (14) (Israel-English)	Etomidate (any dose) vs. other sedatives	Subgroup of double-blind RCT	65 [57–74]	499	66.5	SAPS II (48 [37–62])	All-cause 28-day mortality	41 (42.7)	123 (30.5)	4	Randomization; blinding
Tekwani et al/ 2009 (17) (USA-English)	Etomidate vs. other sedatives	Prospective observational cohort	77 [68–84]	106	45.3	Mortality in the Emergency Department of Sepsis (13 [10–16])	All-cause in-hospital mortality	28 (38.0)	14 (43.7)	1	Inclusion/ exclusion criteria; follow-up; adverse effects
Jabre et al/2009 (5) (French-English)	Etomidate (0.3 mg/kg) vs. ketamine (2 mg/kg)	Single-blind RCT	57.9 ± 18.6	76	59.7	SAPS II (50.9 ± 17.9)	All-cause 28-day mortality	17 (41.5)	12 (34.3)	5	Follow-up
Tekwani et al/ 2010 (16) (USA-English)	Etomidate (0.3 mg/kg) vs. midazolam (0.1 mg/kg)	Double-blind RCT	72 [60–82]	122	22.1	SAPS II (54 ± 16)	All-cause in-hospital mortality	26 (36)	21 (43)	7	None
Cherfan et al/ 2011 (22) (Saudi Arabia-English)	Etomidate (20 mg) vs. other sedatives	Subgroup of double-blind RCT	61.0 ± 12.0	62	59.7	Sequential Organ Failure Assessment (15.2 ± 3.3)	All-cause 28-day mortality	21 (91)	33 (84)	6	Randomization

Mortality

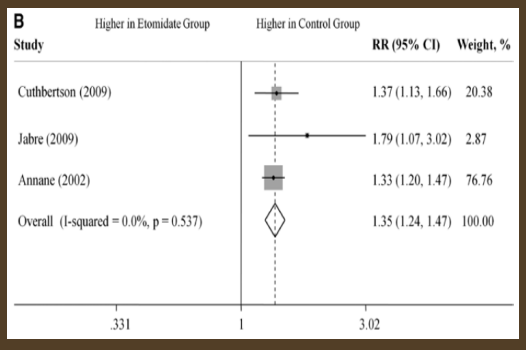


Adrenal Insufficiency

Table 2. Studies included for adrenal insufficiency

Study/Year (Country-Language)	Intervention	Design	Age, yrs[a]	Patients, n	Male Gender, %	Severity of Illness (Score)[a]	End Point [Time Frame for AI Testing After Etomidate Dose]	AI in Etomidate Group, n (%)	AI in Comparison Group, n (%)	Quality Score	Quality Problems
Cuthbertson et al/2009 (14) (Israel-English)	Etomidate (any dose) vs. other sedatives	Subgroup of double-blind RCT	65 [57–74]	499	66.5	SAPS II(48 [37–62])	AI by CST (60 mins after 0.25 mg tetracosactrin) [within 72 hrs]	58 (61.0)	175 (44.6)	4	Randomization; blinding
Jabre et al/2009 (5) (French-English)	Etomidate (0.3 mg/kg) vs. ketamine (2 mg/kg)	Single-blind RCT	57.9 ± 18.6	46	59.7	SAPS II(50.9 ± 17.9)	AI by CST (30 and 60 mins after cosyntropin) [within 48 hrs]	21 (80.1)	9 (45.0)	5	Follow-up
Kim et al/2008 (18) (Korean-English)	Etomidate (0.3 mg/kg) vs. midazolam (0.07 mg/kg)	Single-center retrospective cohort	63.6 ± 13.3	65	72.3	Acute Physiology and Chronic Health Evaluation II (27.0 ± 5.9)	AI by CST (0.25 mg tetracosactrin) [within 24 hrs]	21 (84.0)	19 (48.0)	3	Randomization; follow-up
Mohammad et al/2006 (19) (USA-English)	Etomidate vs. other sedatives	Single-center retrospective cohort	60.1 ± 17.3	152	54.6	None	AI by CST (30 and 60 mins after cosyntropin) [at least 24 hrs after etomidate]	29 (76.0)	58 (51.0)	3	Randomization; follow-up
Dmello et al/2010 (15) (USA-English)	Etomidate (0.3 mg/kg) vs. other sedatives	Single-center retrospective cohort	64.5 ± 18.0	126	54.9	Acute Physiology and Chronic Health Evaluation II (21.6 ± 8.2)	AI by CST (30 and 60 mins after 0.25 mg cosyntropin), random cortisol level [within 72	16 (24.0)	13 (22.0)	2	Randomization; follow-up; inclusion/exclusion

Adrenal Insufficiency



Discussion and Conclusion

- Long term effects of etomidate not been evaluated yet
- Etomidate in pt with sepsis associated with higher mortality (1.2X) and AI
- Etomidate should be warranted when in use

Limitation

- Meta-analysis, confounders
- Etiology of AI, definition of AI
- Mortality evaluated differed between studies