Journal reading

2013/4/23

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Endogenous carboxyhemoglobin concentrations in the assessment of severity in patients with community-acquired pneumonia

Seref Kerem Corbacioglu MD et al,

American Journal of Emergency Medicine 31 (2013) 520–523

Outlines

- **Introduction**
- **Method**
- **Result**
- **Discussion**
- **Limitation**
- **Conclusion**

Introduction-Background

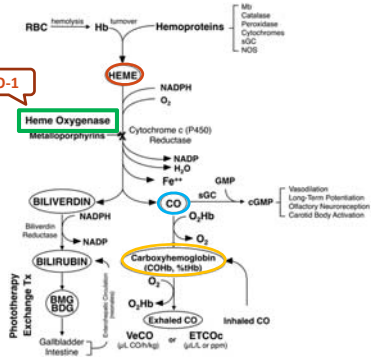
- Community-acquired pneumonia
  - High morbidity and mortality
  - Severity➔ management
- Carbon oxide
  - Produce endogenously during HEME reduction
- HEME oxygenase-1
  - Respiratory epithelial cells
  - Endothelial cells
  - Alveolar macrophages

Introduction-Background

Oxidative stress
Hypoxia
Inflammation
Heavy metals

stimulate

HO-1



- COHb
  - ↑in pneumonia-related inflammation & hypoxic stress

Ref. www.frontiersin.org

Introduction-Importance

- Scoring systems
  - Pneumonia severity index
  - CURB-65

↓

- Inefficiently
  - Overcrowding
  - Difficulty in immediate decision

↓

- Easier Scores & indicator
  - Endogenous CO➔ COHb

Introduction-Goals

- Whether endogenous CO levels in CAP were ↑ compared with control group
- Whether COHb concentrations could predict severity of pneumonia in CAP patients by means of comparing pneumoinia scoring systems

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Materials and methods

- Study design
  - Prospective cross-sectional study
  - Urban tertiary care university
  - 55000 visits in 2011/6~2012/3 (10 months)
- Inclusion criteria
  - Age: >=18 with CAP
  - Absence of exclusion criteria →
    - Age <18 years
    - Current smokers
    - Hematological disorders
    - Autoimmune diseases
    - CO poisoning
    - Health care–associated pneumonia
    - Hospital-acquired pneumonia
    - Ventilator-acquired pneumonia

Materials and methods

- CAP
  - New onset infiltrates on CXR
  - Fever
  - Chest symptoms
  - Abnormal PE signs
- Control group
  - No resp. or CV disease
  - Current non-smokers

Materials and methods

- Data collection
  - Demographic characteristics
  - Medical comorbidities
  - Smoking history
  - Vital signs, PE, excluding criteria, lab, imaging
  - Antibiotic regimens
  - Admissions or discharge decisions
  - Glasgow Coma Scale scores, PSI, and CURB-65 scores

Materials and methods

- Measurement of COHb
  - Arterial blood
- Statistical analysis

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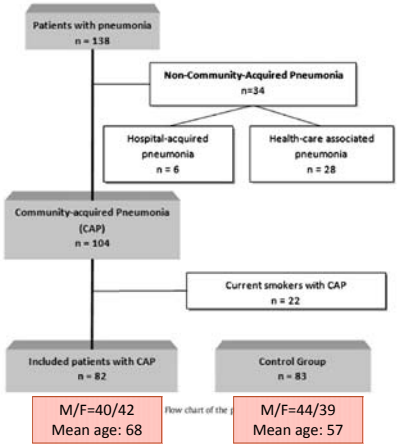
Result



M/F=40/42
Mean age: 68

M/F=44/39
Mean age: 57

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Result

- COHb

	Pneumonia	Control
N	82	83
COHb	1.7% (0.8-3.2)	1.4% (0.8-2.9)

- Baseline charateristics

Patients' characteristics and relation to COHb concentrations

Comorbidity		n (%)	COHb (%) median (minimum-maximum)	P
DM	Yes	26 (31.7)	1.55 (1.0-3.2)	.221
	No	56 (68.3)	1.70 (0.8-3.2)	
Hypertension	Yes	34 (41.5)	1.65 (1.0-2.3)	.406
	No	48 (58.5)	1.70 (0.8-3.2)	
Heart failure	Yes	11 (13.4)	1.70 (1.2-2.5)	.886
	No	71 (86.6)	1.70 (0.8-3.2)	
COPD	Yes	23 (28.0)	1.70 (1.0-3.1)	.333
	No	59 (72.0)	1.60 (0.8-3.2)	
Malignancy	Yes	8 (9.8)	1.95 (1.0-2.3)	.402
	No	74 (90.2)	1.65 (0.8-3.2)	

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Result

- PSI and CURB-65

Distribution of PSI and CURB-65 score categorizations according to patients' hospitalization/discharge and COHb levels

	Hospitalization, n (%)	Discharged, n (%)	Total, n (%)	COHB (%) median (minimum-maximum)
PSI				
Low	24 (55.8)	19 (44.2)	43 (52.4)	1.60 (0.8-3.2)
Moderate	30 (90.9)	3 (8.1)	33 (40.2)	1.80 (1.1-3.1)
High	6 (100)	0 (0)	6 (7.4)	1.85 (1.1-2.3)
CURB-65				
Low	31 (60.7)	20 (39.3)	51 (62.2)	1.60 (0.8-3.2)
Moderate	22 (91.6)	2 (8.4)	24 (29.3)	1.75 (1.2-3.2)
High	7 (100)	0 (0)	7 (8.5)	1.80 (1.1-2.3)
Total	60 (73.1)	22 (26.9)	82 (100)	

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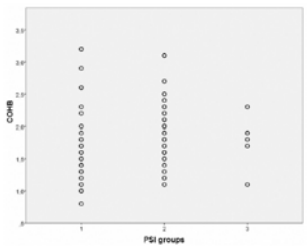
Result

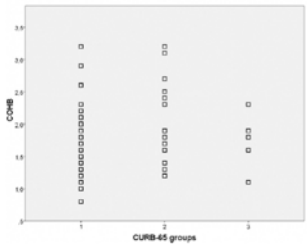
- Distributions of COHb levels of the patient according to the

PSI



P=.04
R=0.187

CURB-65



P=.218
R=0.112

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Result

- Cutoff levels
  - Difference between groups requiring hospitalization or not according to the PSI

COHb	Sensitivity	Specificity
1.650%	64%	58%
1.750%	56%	69%

  - The area under the curve=0.636 (P=.034)
- All patients
  - 26.9% (n=22): discharged in 24 hrs
  - 73.1% (n=60): hospitalized
  - 2 patient died

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Discussion-1st part

- Starting point
  - How to use COHb levels in clinical practice➔ higher in pulmonary disease in previous studies
- Yasuda et al

	COHb
Control	**0.65% +/- 0.03%**
Asthma	1.13% +/- 0.14%
Pneumonia	1.05% +/- 0.03%
IPF	0.93 +/- 0.03%

  - Significant↓ COHb after steroid in asthma & Abx in pneumonia

- Paredi et al

	Exhaled CO
Control	**2.4 +/- 0.4 ppm**
Cystic fibrosis	6.7 +/- 0.6 ppm

- Yamara et al

	Exhaled CO
Stable asthma	**1.4 +/- 0.2 ppm**
Asthma attack	4.6 +/- 0.4 ppm

  - ↓in weekly postattack

- Yasuda et al

	COHb
Control	**0.55 +/- 0.02 %**
Stable COPD	**0.81 +/- 0.02 %**

	COHb
Control	**0.6~0.8 %**
Pneumonia	1.0~1.2 %

- This study
  - ↑COHb level in pneumonia (1.7 vs 1.4%)
    - ➔Relationship between ↑COHb & pulmonary disease with hypoxic & inflammatory condition
  - Not clear to use in clinical practice
  - Evaluating COHb levels alone
    - ➔ not enough to diagnose/ support diagnosis

Discussion-2nd part

- Clinical severity of the pneumonia with correlation of PSI & CURB-65
  - No direct study between COHb & PSI
  - Yasuda et al
    - significant correlation between ↑COHb & CRP
  - Chalmers et al
    - critical limit value of CRP=100 mg/dl, sensitivity was higher than PSI
  - Yasuda et al
    - Positive correlation in COHb with WBC

- In our study
  - No correlation with CURB-65
  - Weak positive correlation with PSI

  ➔COHb levels proven to be increased in patients with pneumonia is not a reliable indicator in predicting clinical severity

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Limitation

- Mean ages of patients & control groups
- De Siqueira et al
  - no relationship between age and COHB levels control groups

Age	COHb
15~25	1.12 %
25~35	0.78%
Older	0.90%

  - ➔ minor significance

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Conclusion

- Although COHb levels ↑in patients with pneumonia, we cannot conclude that this increase acts as an indicator in diagnosis process or prediction of clinical severity for the physician

Red cell distribution width is a prognostic factor in severe sepsis and septic shock

You Hwan Jo MD, PhD et al.,
American Journal of Emergency Medicine 31 (2013) 545–548

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- **Introduction**
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Introduction

- Severe sepsis & septic shock
  - ↑incidence, mortality rate
  - Prediction of outcome
  - Prognostic factors
- Red cell distribution(RDW)
  - Variability of the size of RBC
  - D/D of anemia

Introduction

- Recent studies about RDW
  - Prognosis
    - CHF, AMI, pulmonary embolism, pneumonia, critical illness, cardiac arrest
  - Mechanism: not known
  - Inflammatory markers
    - IL-6, TNF, proinflammatory cytokines
  - In critically ill patients
    - ↑RDW→ associated ↑sepsis & blood stream infection
    - Not focus on septic patients

Introduction

- In this study
  - Hypothesized RDW as inflammation marker
  - Evaluate the relationship between

RDW at admission & 28-day mortality

In patients with severe sepsis & septic shock

Outlines

- **Introduction**
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Method-study population

- Retrospective analysis of prospectively collected patients' data
- Patients: Severe sepsis & septic shock Def.
- Urban, tertiary care, ED
- 2009/1/1~2011/12/31
- 70000 people, > 18 y/o
- Exclusion criteria

Method-study population

- **Surviving sepsis campaign, 2008**
  - Fluid resuscitation with CVP 8 ~ 12 mm Hg
  - Vasoactive agents with MAP of 65 ~ 90 mm Hg
  - RBC transfusion or dobutamine infusion with a CVO2 sat >70%
  - Blood and other sites cultures with broad-spectrum antibiotics
  - Hydrocortisone for refractory shock
  - IV insulin for glucose control 150 ~ 180 mg/dL

Method-Lab

- Blood samples
  - CBC at admission to ED
  - Result in 1 hr
  - Reference range: 11.5~14.5%
  - ABG, serum chemistry, blood cultures

Method-data collection

- Comorbidities
  - DM, HTN, liver disease, COPD
- Initial hemodynamics
  - BP, HR, Temp, primary site of infection, lab, microbiological report
- APACHE II score
- SOFA score
- Outcome variables
  - 28-day mortality, admission to ICU, renal replacement therapy, mechanical ventilation

Method-statistical analyses

- Continuous variables
  - Kolmogorov-Smirmov test
  - Student t test/Mann Whitney test
- Categorial variables
  - X^2 test/Fisher exact test
- Stastistically significant
  - 2 tailed p value < .5

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Result- characteristics

24 pt exclude: withdrawl aggressive management

	Survivors (n = 402)	Nonsurvivors (n = 164)	P
Age (y), median (IQR)	70.5 (62.0-77.0)	75.0 (66.3-83.0)	<.001
Male, n (%)	212 (52.7)	102 (62.2)	.040
Primary site of infection, n (%)			.117
Respiratory	156 (38.8)	101 (61.6)	<.001
Urinary	98 (24.4)	10 (6.1)	<.001
Hepatobiliary	65 (16.2)	20 (12.2)	.230
Gastrointestinal	32 (8.0)	12 (7.3)	.796
Soft tissue	19 (4.7)	4 (2.4)	.211
Miscellaneous	32 (8.0)	17 (10.4)	.356
Comorbidity, n (%)			
Diabetes	122 (30.4)	53 (32.3)	.646
Hypertension	181 (45.0)	80 (48.8)	.416
Liver disease	15 (3.7)	19 (11.6)	<.001
COPD	29 (7.2)	15 (9.2)	.436
Mean arterial pressure (mm Hg), median (IQR)	71.3 (59.3-87.8)	64.5 (54.1-80.7)	.015
Heart rate (beats/min), median (IQR)	108.0 (92.0-125.3)	113.5 (92.3-132.8)	.165
APACHE II score, median (IQR)	17 (12-22)	25 (19-31)	<.001

Result- lab parameters

	Survivors (n = 402)	Nonsurvivors (n = 164)	P
pH	7.425 (7.373-7.454)	7.390 (7.266-7.454)	<.001
White blood cell ($10^3/\mu L$)	11.20 (6.75-16.60)	10.35 (4.97-16.58)	.192
Hematocrit (%)	34.4 (29.6-38.6)	33.0 (28.5-38.2)	.415
MCV (fL)	94.0 (90.8-97.9)	96.1 (92.5-100.4)	<.001
MCH (pg)	31.9 (30.6-33.3)	32.1 (30.5-33.6)	.509
RDW (%)	14.4 (13.5-15.8)	15.8 (14.5,17.0)	<.001
Platelet ($10^3/\mu L$)	166 (108-235)	155 (76-255)	.303
Sodium (mmol/L)	135 (132-139)	135 (130-140)	.539
Potassium (mmol/L)	4.0 (3.6-4.6)	4.4 (3.7-5.0)	.001
BUN (mg/dL)	25 (17-37)	34 (22-51)	<.001
Creatinine (mg/dL)	1.2 (0.9-1.9)	1.4 (0.9-2.3)	.009
Cholesterol (mg/dL)	125.5 (100.0-157.0)	104.5 (84.0-132.5)	<.001
Albumin (mg/dL)	3.3 (2.8-3.6)	2.8 (2.4-3.1)	<.001
CRP (mg/dL)	13.3 (5.4-22.0)	15.2 (6.8-22.0)	.106

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Result- outcomes by RDW

	RDW			P
	≤14% (n = 198)	14.1%15.7% (n = 183)	≥15.8% (n = 185)	
Mortality, n (%)	26 (13.1)	55 (30.1)	83 (44.9)	<.001
APACHE II score, median (IQR)	15 (11-21)	20 (14-26)	21 (16-27)	<.001
SOFA score, median (IQR)	6 (5-9)	7 (5-10)	9 (6-11)	<.001
Renal replacement therapy, n (%)	9 (4.6)	16 (8.7)	13 (7.0)	.257
Mechanical ventilation, n (%)	48 (24.2)	59 (32.2)	58 (31.4)	.166
Admission to ICU, n (%)	60 (30.3)	60 (32.8)	63 (34.1)	.726
Positive blood culture, n (%)	79 (39.9)	72 (39.3)	78 (42.2)	.842

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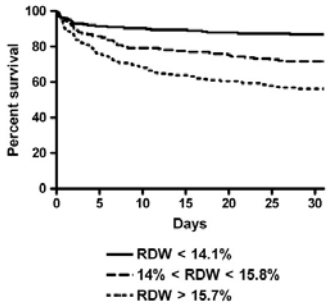
Kaplan-Meyer survival curve of patients with severe sepsis and septic shock



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Cox proportional hazards regression analysis for 28-day mortality

	Adjusted hazard ratio	95% CI	P
Age	1.02	1.00-1.04	.034
Male	1.26	0.88-1.79	.212
Primary site of infection			
Respiratory	1.09	0.72-1.66	.672
Urinary	0.38	0.19-0.79	.010
Liver disease	2.55	1.10-4.65	.002
Mean arterial pressure	1.00	0.99-1.01	.609
pH	0.94	0.93-0.96	<.001
White blood cell	0.99	0.99-1.01	.581
Hematocrit	1.01	0.99-1.03	.431
MCV	0.97	0.92-1.02	.195
MCH	1.09	0.96-1.23	.208
Potassium	0.99	0.98-1.01	.536
Blood urea nitrogen	1.01	1.00-1.02	.028
Creatinine	0.98	0.96-0.99	.008
Cholesterol	0.99	0.99-1.01	.768
Albumin	0.91	0.88-0.95	<.001
APACHE II score	1.05	1.02-1.08	<.001
RDW (%)			
≤14	Reference		
14.1-15.7	1.66	1.00-2.76	.049
≥15.8	2.57	1.53-4.34	<.001

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Result

- Most common microorganism
  - **G(+)**: Coagulase(-) Staphylococcus, S. aureus, S, pneumoniae
  - **G(-)**: E. coli, K. pneumoniae, P. aeruginosa
  - No difference in the rate of B/C(+) & RDW

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Discussion

- In this study
  - ↑RDW of nonsurvivors in severe sepsis & septic shock
  - Graded association in 28-day mortality
- Previous studies
  - General CV disease
  - Critically ill patients
    - ↑RDW, ↑sepsis rate, ↑blood stream infection

➔This is the 1st study to evaluate the association of RDW with outcomes in severe sepsis & septic shock

Discussion

- **Mechanism**
  - Uncertain
  - RBC is produced ineffectively or increasingly destructed
  - Proinflammatory cytokines
  - Oxidative stress & neurohormonal responses

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Limitation

- Retrospective analysis in a single institution
- RDW could be influenced by iron, folate and vit. B12
- Transfusion records before admission are not available
- Association =\= causality

Strength

- Patients were included consecutively
- Managed following guidelines
- RDW were measured initially irrespective of diagnosis and severity
- Severity score were evaluated

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Conclusion

- Red cell distribution width at admission is associated with 28-day mortality and severity of patients with severe sepsis and septic shock
- RDW could be used as a prognostic factor

Thank you ☺