

Association of Physical Examination with
Pulmonary Artery Catheter Parameters in
Acute Lung Injury

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Outline

- Clinical Study
 - Method
 - Results
- Discussion
 - Internal Validation
 - External Validation

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Clinical Study Method

- Background
 - Clinical value of PAC insertion in ALI patients
 - Physical examination as a substitute for PAC

The graph displays the proportion of patients alive over a 60-day period. The y-axis represents the 'Proportion of Patients' from 0.0 to 1.0. The x-axis represents 'Days' from 0 to 60. Four curves are shown: 'Alive, PAC group' (top curve, starting at 1.0 and ending near 0.8), 'Unassisted breathing, CVC group' (second curve from top, starting at 1.0 and ending near 0.7), 'Unassisted breathing, PAC group' (third curve from top, starting at 0.0 and ending near 0.7), and 'Alive, CVC group' (bottom curve, starting at 0.0 and ending near 0.6). The 'Unassisted breathing, PAC group' curve crosses the 'Unassisted breathing, CVC group' curve around day 15.

NEJM, 2006, FACTT

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- NEJM, 2006, FACTT



Clinical Study Method

- Design
 - Retrospective study
 - Post-hoc analysis of FACTT

The diagram illustrates a post-hoc analysis of the FACTT study. A red circle highlights the 'Ineffective Circulation' section in the table, and a red arrow points from this circle to a magnified view of the same section on the right.

Measure of intracranial pressure (mm Hg)				Measure of intracranial pressure (mm Hg)			
Control group	Intervent group	Control group	Intervent group	Control group	Intervent group	Control group	Intervent group
Range 1				Range 2			
1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Range 3				Range 4			
1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Range 5				Range 6			
1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Ineffective Circulation

Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec

Effective Circulation

Cardiac index ≥2.5 liters/min/m² and warm, pink skin with capillary-refilling time ≤2 sec

Death

Death due to any cause

Survival

Survival at 90 days

Quality of Life

Quality of Life at 90 days

Adverse Events

Adverse Events at 90 days

Statistical Analysis

Statistical Analysis at 90 days

Conclusion

Conclusion at 90 days

NEJM, 2006, FACTT

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- | Measure of intracranial pressure (mm Hg) | | | | Measure of intracranial pressure (mm Hg) | | | |
|--|-----------------|---------------|-----------------|--|-----------------|---------------|-----------------|
| Control group | Intervent group | Control group | Intervent group | Control group | Intervent group | Control group | Intervent group |
| Range 1 | | | | Range 2 | | | |
| 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Range 3 | | | | Range 4 | | | |
| 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
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- Ineffective Circulation**
- Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec
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- Death**
- Death due to any cause
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- Statistical Analysis at 90 days
- Conclusion**
- Conclusion at 90 days
- NEJM, 2006, FACTT

NEJM, 2006, FACTT[illegible]

Cardiac index

skin with capillary-refilling times ≥ 2 s.

3 KVO IV
Dobutamine^A

Clinical Study Method

- FACTT Study Design

```

graph TD
    A[Randomized] --> B[Acute Onset  
within 24h  
of randomization  
n=100  
n=100]
    A --> C[No Acute Onset  
within 24h  
of randomization  
n=100  
n=100]
    B --> D[Group 1  
Hypoxemia  
criterion #1  
n=50  
n=50]
    B --> E[Group 2  
Hypoxemia  
criterion #2  
n=50  
n=50]
    C --> D
    C --> E
    D --> F[Mortality  
n=100  
n=100]
    E --> F
    
```

4.2 Inclusion Criteria

Acute Onset of:

1. $\text{PaO}_2/\text{FiO}_2 \leq 300$. If altitude $> 1000\text{m}$, then $\text{PaO}_2/\text{FiO}_2 \leq 300 \times (\text{B.P.}/760)$.
2. Bilateral infiltrates consistent with pulmonary edema on frontal chest radiograph. The infiltrates may be patchy, diffuse, homogeneous, or asymmetric.
3. Requirement for positive pressure ventilation via endotracheal tube.
4. No clinical evidence of left atrial hypertension.

Criteria 1-4 must occur together within a 24-hour interval.

"Acute Onset" is defined as follows: the duration of the hypoxemia criterion (#1) and the chest radiograph criterion (#2) must be ≤ 28 days at the time of randomization.

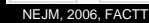
NEJM, 2006, FACTT

NEJM, 2006, FACTT, supp. data

- # Clinical Study Method
- FACTT Study Design
-
- ```

graph TD
 A[Randomized] --> B[Acute Onset
within 24h
of randomization
n=100
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 A --> C[No Acute Onset
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n=100
n=100]
 B --> D[Group 1
Hypoxemia
criterion #1
n=50
n=50]
 B --> E[Group 2
Hypoxemia
criterion #2
n=50
n=50]
 C --> D
 C --> E
 D --> F[Mortality
n=100
n=100]
 E --> F

```
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- Acute Onset of:**
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## Louis-Quint, of

1. B. G. (1970)

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NEJM, 2006, FACTT, supp. data

# Clinical Study

## Method

- Objectives
  - Association of **physical findings** with  $CI < 2.5$  or  $SvO_2 < 60\%$
  - Association of **physical findings** and 24hr **fluid output** and **CVP** with  $CI < 2.5$  or  $SvO_2 < 60\%$
  - Correlation of  $ScvO_2$  and  $SvO_2$

- # Clinical Study
- ## Method
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## Clinical Study Result 1

| Table 1. Presence of all three physical examination findings (capillary refill >2 sec, knee mottling, and cool extremities) as predictors of CI <2.5 |                   |                   |                                 |
|------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------|---------------------------------|
| N = 405                                                                                                                                              | CI <2.5           | CI ≥2.5           |                                 |
| All 3 physical examination findings present                                                                                                          | 4                 | 6                 | Positive predictive value = 40% |
| All 3 not present                                                                                                                                    | 29                | 364               | Negative predictive value = 92% |
|                                                                                                                                                      | Sensitivity = 32% | Specificity = 98% |                                 |

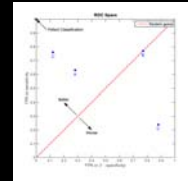
| Table 2. Presence of any one physical examination finding (capillary refill >2 sec, knee mottling, or cool extremities) as predictors of CI <2.5 |                   |                   |                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------|---------------------------------|
| N = 405                                                                                                                                          | CI <2.5           | CI ≥2.5           |                                 |
| Any 1 physical examination finding present                                                                                                       | 17                | 83                | Positive predictive value = 17% |
| No physical examination findings present                                                                                                         | 16                | 289               | Negative predictive value = 93% |
|                                                                                                                                                  | Sensitivity = 52% | Specificity = 78% |                                 |

| Test | Disease |     |
|------|---------|-----|
|      | (+)     | (-) |
| (+)  | a       | b   |
| (-)  | c       | d   |

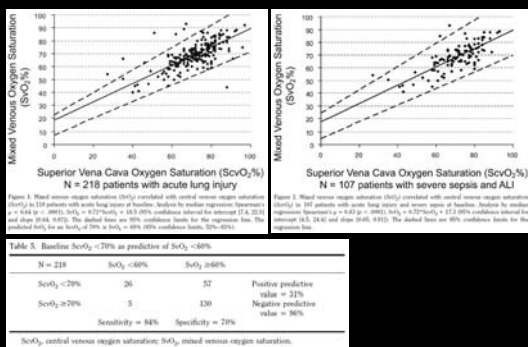
Sen= a/(a+c) pre-test probability= prevalence  
 Spe= d/(b+d) post-test probability= PPV or 1-NPV  
 PPV= a/(a+b) LR+ = sen/1-spe  
 NPV= d/(c+d) LR- = 1-sen/spe  
 Prevalence= (a+c)/(a+b+c+d)

## Clinical Study Result 2

- CI<2.5 and cool extremities:
  - OR= 1.9 (p=1.0)
- CI<2.5 and high CVP:
  - OR= 1.06/1cm H<sub>2</sub>O (p=0.002)
- CI<2.5 and low fluid output:
  - OR= 0.8/1L (p= 0.01)
- SvO<sub>2</sub><60% correlated with:
  - knee mottling (OR= 5.0, p= 0.09) and high CVP (OR= 1.09/1cmH<sub>2</sub>O, p= 0.004)
- No clinical results via ROC analysis



## Clinical Study Result 3



## Discussion

- 3 questions about diagnostic tests:
1. Is the evidence valid (internal validity)
  2. Does the evidence show that the test can distinguish patients with or w/o the disorder (internal validity)
  3. Can I apply the test to a specific patient (external validity)

## Discussion Internal Validation

**Table 3.2** Is this evidence about a diagnostic test valid?

1. **Measurement:** was the reference ("gold") standard measured independently, i.e. blind to our target test?
  2. **Representative:** was the diagnostic test evaluated in an appropriate spectrum of patients (like those in whom we would use it in practice)?
  3. **Ascertainment:** was the reference standard ascertained regardless of the diagnostic test result?
- (Fourth question to be considered for clusters of tests of clinical prediction rules: was the cluster of tests validated in a second, independent group of patients?)

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## Discussion Internal Validation

- SnNout and SpPin
- Pre-test probability and post-test probability
- Youden Index

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|                                                                                                                                                  | Sensitivity = 52% | Specificity = 78% |                                 |

CI<2.5 prevalence= 8.1%

SvO<sub>2</sub><60% prevalence= 15.5%

## Discussion External Validation

**Table 3.5** Questions to answer in applying a valid diagnostic test to an individual patient

1. Is the diagnostic test available, affordable, accurate, and precise in our setting?
2. Can we generate a clinically sensible estimate of our patient's pre-test probability?
  - From personal experience, prevalence statistics, practice databases, or primary studies?
  - Are the study patients similar to our own?
  - Is it unlikely that the disease possibilities or probabilities have changed since this evidence was gathered?
3. Will the resulting post-test probabilities affect our management and help our patient?
  - Could it move us across a test-treatment threshold?
  - Would our patient be a willing partner in carrying it out?
  - Would the consequences of the test help our patient reach his or her goals in all this?

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## Discussion External Validity

- Consistency of physical examinations
- Knee mottling?

| Mild<br>(<20% Blood Volume)                                                                         | Moderate<br>(20-40% Blood Volume)                                       | Severe<br>(>40% Blood Volume)                                                                                        |
|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| Cool extremities<br>Increased capillary<br>refill time<br>Diaphoresis<br>Collapsed veins<br>Anxiety | Same, plus:<br>Tachycardia<br>Tachypnea<br>Oliguria<br>Postural changes | Same, plus:<br>Hemodynamic instability<br>Marked tachycardia<br>Hypotension<br>Mental status<br>deterioration (coma) |

Harrison's 16<sup>th</sup> ed.

16. Signs of effectiveness of the arterial circulation (capillary refill time, knee mottling, skin temperature, etc.)

NEJM, 2006, FACTT, supp. data

## Discussion External Validation

| Exclusion Criteria                                                                       | Exclusion Criteria                                                                                                                                                                | Exclusion Criteria              |
|------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| 1. Presence of a PFT at any time after onset of ALL (meeting of inclusion criteria 1-4). | 2. Age < 13 years.                                                                                                                                                                | 3. Age > 80% body surface area. |
| 4. > 40 hours after onset of ALL (meeting of inclusion criteria 1-4).                    | 5. Not consented to full report (Exception: a patient will not be excluded if he/she would receive all supportive care except for attempts at resuscitation from cardiac arrest). | 6. Brain tumor resection.       |
| 7. Brain tumor resection.                                                                | 8. Brain tumor resection.                                                                                                                                                         | 9. Brain tumor resection.       |
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| 98. Brain tumor resection.                                                               | 99. Brain tumor resection.                                                                                                                                                        | 100. Brain tumor resection.     |

NEJM, 2006, FACTT

### Exclusion Criteria

1. Presence of a PFT at any time after onset of ALL (meeting of inclusion criteria 1-4).
2. Age < 13 years.
3. Age > 80% body surface area.
4. > 40 hours after onset of ALL (meeting of inclusion criteria 1-4).
5. Not consented to full report (Exception: a patient will not be excluded if he/she would receive all supportive care except for attempts at resuscitation from cardiac arrest).
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NEJM, 2006, FACTT, supp. data

## Conclusion

- Physical examination (capillary refill, cool skin, or knee mottling) are not clinically useful to predict low CI or SvO<sub>2</sub>.
- ScvO<sub>2</sub> significantly correlates with SvO<sub>2</sub>, but with wide confidence interval, and thus its clinical value is uncertain.

## Questions and Comments



Perceived Barriers to Therapeutic Hypothermia for Patients Resuscitated from Cardiac Arrest

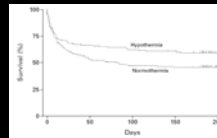
## Clinical Study

- Background
  - Benefit from therapeutic hypothermia (TH) demonstrated in RCTs and meta-analysis
  - TH incorporated into AHA guideline
  - Only 26% of physicians regularly institute TH protocol

Table 2. Neurologic Outcome and Mortality at 90 Minutes

| Outcome                 | Hypothermia  | Normothermia | Risk Ratio (95% CI)* | P Value† |
|-------------------------|--------------|--------------|----------------------|----------|
| Good neurologic outcome | 54/117 (46%) | 75/134 (56%) | 1.40 (1.00–1.95)     | 0.049†   |
| Death                   | 79/130 (61%) | 54/117 (46%) | 0.76 (0.50–0.95)     | 0.02†    |

NEJM, 2002, Hypothermia after Cardiac Arrest Study Group



## Clinical Study Method

- **Qualitative** study design
- Semi-structured personal interviews
- **Purposeful** random sampling
  - Sampling from 14 hospitals (include community hospitals and centers)
  - More nurses and physicians from ED
  - Snowball sampling
- Total of 21 interviews (4 ICU physician, 7 ED physician, 10 nurses)

## Clinical Study Method

Table 1. Interview guide

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>Knowledge</b></p> <p>How would you describe your current knowledge or level of understanding of mild TH for post-arrest patients?</p> <p><b>Practices</b></p> <p>Are you aware of the guidelines for TH?</p> <p>How would you describe the knowledge level of your colleagues in ICU/EDs?</p> <p>Has your institution provided training on the use of TH?</p> <p>What is your reading of the attitudes of your colleagues (if nurses/physicians) in the ICU/ED regarding TH?</p> <p><b>Attitudes</b></p> <p>What are your current views on the use of TH for cardiac arrest patients?</p> <p>What is the evidence?</p> <p>What are the outcomes?</p> <p>In your view, how feasible is the use of TH in your hospital?</p> <p>Are there guidelines on this?</p> <p>Are there any cost issues?</p> <p><b>Barriers to guideline adoption</b></p> <p>Is TH currently in use at your institution?</p> <p>If no, to what extent has it been implemented institutionally?</p> <p>If not, was it considered and decided against? Not considered? Will be considered?</p> <p>How would you describe your experience with TH?</p> <p>How do you use it in your practice?</p> <p>How are patients cared in your institution?</p> <p>What have been indicated low uptake of TH. In your view, what are the barriers to its use?</p> <p>Are there limited resources? Time barriers? Patient barriers? Staff barriers?</p> <p>How thinking institutionally about your practice/department/hospital, what are the barriers you've encountered?</p> <p>What would facilitate the use of TH in your practice/department/hospital?</p> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

TH, therapeutic hypothermia; ICU, intensive care unit; ED, emergency room.

## Results

- Barriers to TH
  - **Awareness:** lack of awareness of nurses in small community hospitals
  - **Agreement:** limited RCTs, uncertain risk/benefit
  - **Adoption/Adherence:** variably adopted among individuals, especially in ED. Inconsistency between ICU and ED, physicians and nurses.
  - Process Issues: equipment, cost, and workload
  - Lack of experience (rare)

## Discussion

- Internal Validation
  - Behavior change model
  - Value of a qualitative study
- External Validation
  - Comparable to other scenarios of implementing novel intervention strategies
  - Application to a different country (numerous issues of concern, e.g. culture, economy, politics, insurance...etc)

## Conclusion

- Systemic adoption of TH is met with many physical barriers.
- Future studies are needed to determine which implementation strategy may improve uptake of TH.

## Questions and Comments



No need to fear a little freeze