Biomarker & Herzinsuffizienz

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Disclosures

• Swiss National Science Foundation

• University Hospital Basel

• Abbott, Alere, Beckman Coulter, BG Medicine, Bühlmann, Brahms, Critical Diagnostics, Roche, Schiller, Siemens, Novartis, Cardiorentis
Do we really need biomarkers in HF?

1) Yes

2) No
Biomarker: Tool

HF doctor: Task

1) Accurate diagnosis
2) Symptoms ↓ from HF
3) Mortality ↓ from HF
4) Detect & manage comorbidities
1. Diagnosis of HF
2. Phenotype of HF
3. Monitoring HF Treatment
4. Diagnosis of comorbidities
1. Is it AHF? History, physical, ECG
   Chest x-ray, BNP ✓

2. Cardiac disease?

3. Trigger?
Acute Dyspnea: difficult diagnosis

DD: >20 Disorders

50%  
50%

Acute Heart Failure

COPD / Asthma

Pulm. Embolism

Pneumonia
  Tumor
  ILD
  Pneumothorax

Anxiety

Anemia
  Metabol. Acidosis
  ........

Acute Dyspnea: Difficult Diagnosis

Delay in adequate treatment
→ Morbidity ↑
→ Cost ↑

Patients (n)

Probability for Heart Failure

NPs: Quantitative Marker of HF

Volume \uparrow \\
Pressure \uparrow \\

LV Syst. Dysfunction 
+ 
LV Diast. Dysfunction 
+ 
Valvul. Dysfunction 
+ 
RV Dysfunction

1) Diagnosis 
2) Disease Severity

NP improve diagnostic accuracy

- Combined: Area Under ROC Curve = 0.86 (0.84-0.88)
- BNP: Area Under ROC Curve = 0.90 (0.88-0.91)
- E.D. Probability: Area Under ROC Curve = 0.93 (0.92-0.94)
BNP improves patient management

Hospitalisations ↓
ICU ↓
Days in hospital ↓
Cost ↓

Cut-off levels: The accuracy of NP can be increased by adjusting for:

1. Gender
2. Coronary artery diseases
3. Obesity
Obesity: does it matter?
Obesity: Optimal cut-off levels to rule out HF

[Graph showing BNP levels for different BMI categories]

Interpretation of BNP in Acute Dyspnea

1) Quantitative Variable

2) Always conjunction with clinical information

<100pg/ml*

↓

No CHF

100-400pg/ml

↓

Additional information

↓

No CHF

>400pg/ml

↓

CHF

↓

Diuretics

Nitrates

ACE-I

*Cave: a) GFR < 60ml/min

b) Obesity

Triggers of AHF

1. Malcompliance with medication +/- salt/water
2. Co-Medication (NSAR, Glitazone, Isoptin, Sotalol)
3. Hypertensive crisis
4. Systemic Infections (CRP, PCT)
5. Acute Myocardial Infarction (cTn), Ischemia
6. Arhythmia (tachycardiac atrial fib)
7. Pulmonary embolism (D-Dimers)
8. New valvular lesion
9. Anemia (Hb, Ferritin, Transferinsättigung)
10. Hypo/Hyperthyreodism (TSH)
Sepsis is the trigger of >25% of AHF episodes
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32,229 Hospitalization Episodes in Validation Cohort

BUN <43 mg/dL
- 2.83% Crude Mortality (704/24,871)
  - 24,702 Hospitalization Episodes
    - Systolic Blood Pressure ≥115 mm Hg
      - Low Risk
        - 2.31% Crude Mortality (480/20,820)
    - Systolic Blood Pressure <115 mm Hg
      - Intermediate Risk 3
        - 5.67% Crude Mortality (220/36,822)

BUN ≥43 mg/dL
- 8.35% Crude Mortality (565/67,764)
  - 65,977 Hospitalization Episodes
    - Systolic Blood Pressure ≥115 mm Hg
      - Intermediate Risk 2
        - 5.63% Crude Mortality (272/46,342)
    - Systolic Blood Pressure <115 mm Hg
      - Intermediate Risk 1
        - 13.23% Crude Mortality (168/1,270)

- Serum Creatinine <2.75 mg/dL
- Serum Creatinine ≥2.75 mg/dL
- High Risk
  - 10.76% Crude Mortality (117/592)

RELAX-AHF: Serelaxin

AHF phenotype with impaired renal function (eGFR↓) ➔ mortality↓ from serelaxin vs placebo/diuretics↑

<table>
<thead>
<tr>
<th>eGFR at baseline</th>
<th>Serelaxin (n, %)</th>
<th>Placebo/Diuretics (n, %)</th>
<th>Hazard ratio (95% CI) for CV death through Day 180</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60 mL/min/1.73m²</td>
<td>46/408 (11.5)</td>
<td>25/409 (6.2)</td>
<td>0.53 (0.33, 0.86) 0.1056</td>
</tr>
<tr>
<td>≥60 mL/min/1.73m²</td>
<td>6/160 (3.8)</td>
<td>8/155 (5.2)</td>
<td>1.39 (0.48, 4.00)</td>
</tr>
<tr>
<td>&lt;50 mL/min/1.73m²</td>
<td>37/272 (13.9)</td>
<td>16/268 (6.1)</td>
<td>0.42 (0.23, 0.76) 0.0319</td>
</tr>
<tr>
<td>≥50 mL/min/1.73m²</td>
<td>15/296 (5.1)</td>
<td>17/296 (5.8)</td>
<td>1.14 (0.57, 2.29)</td>
</tr>
</tbody>
</table>
But: Not helpful to detect underlying CAD/Ischemia!!!!
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Change in BNP: AHF is undertreated!!

s.l. & transdermal Nitrates

RELAX-AHF: Serelaxin:

Troponin T (Geometric mean change)

NT-pro-BNP (Geometric mean change)

Cystatin C (Geometric mean change)

Prevention of cardiomyocyte loss

Alleviation of cardiac wall stress and decongestion

Prevention of renal function loss

These changes have shown to be predictive of mortality in AHF

Mehtra M, et al. JACC 2013
Concept of HF Monitoring

- Low BNP, low mortality/morbidity
- If BNP ↓ → risk of death/rehosp ↓
- **Aim:** Maximal ↓ of BNP (without arterial hypoperfusion = Crea↑)

Biomarker to assess **efficacy** (filling pressures)

Biomarker to assess **safety** (organ perfusion)
Does BNP-guidance lower Mortality?

Relative Risk

Troughton
STARBRITE
STARS-BNP
BATTLESARRED
TIME-CHF
PRIMA
Combined

Felker GM et al. Am Heart J 2009
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Biomarkers & HF

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