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VOLUME 2

BIOMARKERS IN CLINICAL USE

NT-pro BNP

Diagnosis and early risk stratification of acute dispnoe and heart failure
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Physical and peptide synthesis differences in the heart with and without heart failure.

Ventricle Stretch

Cleavage by enzyme corin

NT-proBNP

T_{1/2} 1.5 to 2.0 hours Inactive

BNP

T_{1/2} 20 minutes Active Hormone
Emergency heart failure pathway algorithm\(^1\)

- Shortness of breath with possible diagnosis of EHF
  - **YES**: Baseline blood work, CXR, and BNP
    - **YES**: Is patient clinically stable?
      - **NO**: Resuscitate and refer to ICU or CCU
      - **YES**: BNP or NT-pro BNP level*
        - **INDETERMINATE**
        - **POSITIVE**: Is patient well enough for DTU? See Inclusion/Exclusion Criteria
    - **NO**: Consider and treat alternate diagnosis
  - **NO**: NEGATIVE FOR CHF
    - **YES**: Pride score > 7**
    - **NO**: Consider and treat alternate diagnosis
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Refer to CTU, CCU or Cardiology

NT-pro BNP > cut off

Improves and meets discharge criteria by 12 hours after enrollment in Unit?

NT-pro BNP < cut off*

NO

YES

Discharge to appropriate follow-up (GP / Rapid Access / HF clinic)

Enroll in DTU

Abreviations
CxR: Chest x-Ray
DTU: Diagnostic and Treatment Unit
EHF: Emergency Heart Failure
ICU: Intensive Care Unit
CCU: Critical Care Unit

Pride Score
CHF: Cardiac Heart Failure
CTU: Cardiac Treatment Unit
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* BNP or NT-pro BNP level

<table>
<thead>
<tr>
<th>1. EHF Ruled out</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP less than 100</td>
<td></td>
</tr>
<tr>
<td>NT-pro BNP &lt; 300</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. EHF confirmed</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>BNP &gt; 500 any age</td>
<td></td>
</tr>
<tr>
<td>NT-pro BNP:</td>
<td></td>
</tr>
<tr>
<td>• Greater than 450 for age less than 50 y</td>
<td></td>
</tr>
<tr>
<td>• Greater than 900 for age between 50 - 75 y</td>
<td></td>
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<tr>
<td>• Greater than 1800 for age greater than 75 y</td>
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<tr>
<td>BNP and NT-pro BNP greater than 25 percent of the patient’s usual (dry) level</td>
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<thead>
<tr>
<th>3. Indeterminate for EHF</th>
<th></th>
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<tbody>
<tr>
<td>BNP 100-500</td>
<td></td>
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<tr>
<td>NT-pro BNP:</td>
<td></td>
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<tr>
<td>• 300 - 450 for age less than 50 y</td>
<td></td>
</tr>
<tr>
<td>• 300 - 900 for age between 50 - 75 y</td>
<td></td>
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<tr>
<td>• 300 - 1800 for age greater than 75 y</td>
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**Pride Score**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>Elevated NT-pro BNP</td>
<td>4</td>
</tr>
<tr>
<td>Interstitial edema on chest x-ray</td>
<td>2</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>2</td>
</tr>
<tr>
<td>Absence of fever</td>
<td>2</td>
</tr>
<tr>
<td>Current Lop Diuretic use</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>1</td>
</tr>
<tr>
<td>Rales on lung examination</td>
<td>1</td>
</tr>
<tr>
<td>Absence of cough</td>
<td>1</td>
</tr>
</tbody>
</table>
When should NT-pro BNP be measured?\textsuperscript{2}

- to differentiate acute heart failure (HF) from non acute HF
- when patients presenting with acute dyspnoea
- when patients presenting with heart failure
- at time of venipuncture
- for patient risk-stratification prior hospital discharge
- for treatment monitoring of patients with chronic HF
Interpretation of NT-pro BNP levels

NT-pro BNP values to rule out and rule in acute CHF (n = 1256)³

- **NPV = 99%**
  - **PPV = 76%**

- **NPV = 98%**
  - **PPV = 77%**

- **NPV = 88%**
  - **PPV = 82%**

- **NPV = 55%**
  - **PPV = 92%**

- 1800 pg/ml
- 900 pg/ml
- 450 pg/ml
- 300 pg/ml

- age (years)

- **Acute congestive heart failure likely, consider confounding factors**
- **Acute congestive heart failure less likely, alternative causes must be considered**
- **Acute congestive heart failure unlikely**
Why to use NT-pro BNP?

» Improves medical and economic outcome by
  • faster diagnosis with 90 min versus 63 min
  • less hospital admissions of 75% versus 85%
  • shorter time to discharge patient by 8 days versus 11 days
  • cost reduction of 26% and superior judgement than clinical judgement alone

» Cost effectiveness of using NT-pro BNP maintained at 6 months

» Management of patients with chronic HF
A combination of NT-pro BNP testing and standard clinical assessment is superior to either diagnostic modality alone.
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Hospitalization-free survival

Changes in NT-pro BNP levels help determine optimum time for patient discharge.
How to use NT-pro BNP as risk indicator?

Survival rates increases when NT-pro BNP cut off < 300 mg/ml is used for further monitoring of patients.

Kaplan-Meier curves demonstrating the survival rates of all subjects
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NACB recommendation for use of natriuretic peptides (BNP and NT-pro BNP) for determining CVD risk

» Elevated levels increase mortality during next 2 - 7 years

» Good compliance of BNP and NT-pro BNP assays with specifications requested by governments and professional organisations

» Cooperation of laboratories, clinicians, manufactures to work together in education of pre-analytical, analytical and post-analytical issues

» More research needed for identifying patients with increased CVD risk
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Sources

1. Modified: Providence Health Care St. Pauls Hospital, Diagnostic and Treatment Unit / Emergency Department, Emergency Heart Failure Pathway Algorithm


7. NACB Laboratory Medicine Practice Guidelines. Emerging Biomarkers of Cardiovascular Disease and Stroke Draft version 91906