Laboratory Testing for Natriuretic Peptides (NP)-BNP / NT- proBNP

<table>
<thead>
<tr>
<th>Document reference number</th>
<th>CSP031/2019</th>
<th>Document developed by</th>
<th>National Clinical Programme for Pathology</th>
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<td>Clinical Advisory Group for Pathology.</td>
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<td></td>
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<td>National Clinical Advisor and Group Lead.</td>
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<tr>
<td>Approval date</td>
<td>09/2019</td>
<td>Responsibility for implementation</td>
<td>Acute Hospital Division</td>
</tr>
<tr>
<td>Next Revision date</td>
<td>09/2022</td>
<td>Responsibility for review and audit</td>
<td>National Clinical Programme for Pathology</td>
</tr>
</tbody>
</table>
Contents

Key Recommendations for Clinical Users ................................................................. 3
Key Recommendations for Laboratories ................................................................. 3
Background & Epidemiology .................................................................................... 4
Testing ..................................................................................................................... 5
Specimen and Ordering Information ....................................................................... 7
Decision Cut-off Values, Algorithm for Testing & Confounding Factors ............. 7
Information for Patients ......................................................................................... 12
Appendix: Quick Reference Card ........................................................................... 17
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Date & Review Date

Date: September 2019
Review date: September 2022

Scope

This guidance is intended to guide clinicians and clinical laboratories on the appropriate use, result interpretation, performance (diagnostic + analytical) and limitations of testing involving Natriuretic Peptides (NP), BNP or NT-proBNP, in adult non-pregnant patients.

Key Recommendations for Clinical Users

- Measurement of either BNP or NT-proBNP is most useful to support the diagnosis of ambulatory and acute decompensated heart failure (HF), especially in the setting of clinical uncertainty.\(^{(1,2)}\)

- NP levels should always be interpreted within the clinical context and should consider factors which either increase (age, gender [F>M] and other co-morbidities [e.g. renal function]) or decrease levels (obesity, drug therapy [diuretics, beta blockers, ACEi, ARNI etc]).\(^{(3,4)}\)

- BNP/NT-proBNP is not a ‘stand-alone’ test – it is of greatest value when it complements clinical judgement along with other available diagnostic tools. Therefore, to confirm a diagnosis of HF, BNP or NT-proBNP values above their respective ‘rule-out’ thresholds should be correlated with clinical and imaging assessment and non-cardiac causes of increased NP levels excluded.\(^{(5)}\)

Key Recommendations for Laboratories

Methods

- There is currently no difference in diagnostic and prognostic performance between BNP and NT-proBNP.\(^{(6,7,8)}\)

- Provision of an NP assay by point-of-care testing (POCT) e.g. emergency department (ED) or out-patient clinic will depend primarily on whether or not the turnaround time of NP testing by the central laboratory is meeting clinical need. Where this is not met, NP measurement by POCT should be considered, not least in the out-patient setting where the number of follow-up visits may be reduced.\(^{(6)}\) Numerous studies have
compared NP assays available at POCT to those on central laboratory analytical platforms where the majority have shown good correlation in terms of performance and clinical characteristics.\(^{[9,10,11]}\) As for all NP use in Ireland, and especially for POCT testing, models of clinical governance and appropriate reimbursement should be implemented wherever such testing is offered.

- BNP and NT-proBNP test results are not interchangeable and they cannot be directly compared. They have different half-lives, different modes of degradation and critically, different decision cut-off values.\(^{[3,4]}\)

- Laboratories should consult manufacturer’s kit inserts for all information relating to test performance and limitations including cross-reactivities with non-analytes.

**Internal Quality Control (IQC)**

Each Laboratory should implement an IQC programme for BNP or NT-proBNP, in accord with expert opinion including national recommendation.\(^{[14-16]}\) There are no unique requirements for NP IQC procedures. Imprecision targets (total CV) <15% at relevant diagnostic threshold (see later) should be achievable.\(^{[17]}\)

[In a survey of Irish Laboratories the current state of the art imprecision (CV, %) for BNP (Abbott Laboratories + Beckman Coulter) and NT-proBNP (Roche Diagnostics) assays was determined. Overall, the CVs obtained across the analytical range was 2.8 - 11.5 % and 2.2 – 8.0 % for NT-proBNP (50 - 5774 ng/L) and BNP (30 - 2185 ng/L) respectively, as assessed from routine analysis of IQC material (n = 600 - 790).\(^{[17]}\)]

**External Quality Assurance (EQA)**

Each laboratory should participate in an EQA scheme (programme) for BNP or NT-proBNP such as to assure the quality of testing; one which evaluates not only method and participant performance but also provides education, training and support to its participants.\(^{[18]}\)

**Reporting Units**

BNP and NT-proBNP assay results should be reported in ‘conventional’ units: ng/L (or pg/mL).\(^{[17]}\)

**Background & Epidemiology**

The prevalence of HF depends on the definition applied, but is approximately 1–2% of the adult population in developed countries, rising to ≥10% among people > 70 years of age.\(^{[19]}\)

Numerous prognostic markers of death and/or HF hospitalization have been identified in patients with HF. However, their clinical applicability is limited and precise risk stratification in HF remains challenging.\(^{[1]}\)

BNP is synthesised as a pre-hormone (proBNP) comprising 108 amino acids. Upon release into the circulation it is cleaved in equal proportions into the biologically active 32 amino acid BNP, which represents the C-terminal fragment, and the biologically inactive 76 amino acid N-terminal fragment (NT-proBNP).\(^{[20]}\)

BNP has multiple cardiac functions and is released in response to a variety of cardiac stresses, most particularly cardiac stretch.
The severity of HF is usually classified into four classes defined by the New York Heart Association (NYHA) classification system. Plasma BNP and NT-proBNP concentrations are elevated in patients with HF in line with the NYHA class. (4)

NP testing is used currently in the differential diagnosis of dyspnoea, screening for asymptomatic left ventricular dysfunction, risk stratification/prognostication and treatment monitoring in selected patients with HF. (4)

**Testing**

**Who to Test**

Testing for BNP or NT-proBNP may have clinical value in the following circumstances:

1. **Differential diagnosis of dyspnoea where NPs are important adjuncts to clinical assessment, ECG, chest X-ray and echocardiography in patients of suspected HF:**

   **Acute (emergency department):** BNP or NT–proBNP testing improves diagnostic accuracy in patients presenting to the emergency department (ED) with dyspnoea. (3)
   
   [In the Breathing Not Properly (BNP) Multinational Study, B-type natriuretic peptide levels by themselves were more accurate than any other finding in the history, physical finding, or laboratory value in delineating the cause of dyspnoea – B-type natriuretic peptide performed better than either the NHANES or Framingham criteria for diagnosis of congestive HF]. (21)
   
   [A single measurement of serum NPs (BNP or NT-proBNP) is recommended to ‘rule out’ diagnosis in patients presenting with new suspected acute HF]. (22)
   
   [BNP or NT-proBNP levels may guide the intensity of ED treatment, aid in the decision to admit or not admit a patient to the hospital, and clarify the urgency of post-discharge follow-up]. (3)

   **Non-Acute (out-patient, primary care):** BNP or NT-proBNP can be used as an initial diagnostic test in the non-acute setting when echocardiography is not immediately available. (13)

   Elevated natriuretic peptides help establish an initial working diagnosis, identifying those who require further cardiac investigation; patients with values below the cut-point (4) for the exclusion of important cardiac dysfunction do not require echocardiography. (19)

   (a) See Decision Cut-off Values, Algorithm for Testing & Confounding Factors.

2. **Risk stratification and prognosis (in-patients):** BNP or NT-proBNP should be measured routinely at the time of admission and prior to discharge when optivolaemic (dry/baseline) status is achieved.

   [This baseline BNP or NT-proBNP level is likely to be most important in monitoring the patient in the first thirty days after discharge]. (3)

3. **Natriuretic peptide-driven collaborative care in a population at high risk of heart failure (e.g. post MI, diabetes, poorly controlled hypertension).**
In the Irish based STOP-HF Randomized Trial, BNP-based screening and collaborative care among selected patients at high risk of HF resulted in a reduction in the combined rates of left ventricular systolic dysfunction, diastolic dysfunction and HF.\(^{(27)}\)

**Who not to test**

BNP or NT-proBNP testing is not recommended in the following patient cohorts:

1. Patients with classic signs of acute decompensated HF (i.e. prior episodes of ADHF, volume overload, dyspnoea and orthopnoea)\(^{(28)}\) or those with shortness of breath consistent with other aetiologies (i.e. asthma, COPD), BNP is not likely to assist in the diagnostic workup.\(^{(27)}\)

2. Screening for asymptomatic ventricular dysfunction in a low risk population.

3. Monitoring treatment for HF. In general, NPs should not be used to monitor or guide treatment. However for specific patients where monitoring NPs may have value (e.g. <75 years), clinicians should consider the large biological variability when interpreting result changes. For any monitoring of patients on ARNiS, we recommend NT-proBNP. Any such monitoring decisions should be through cardiology consultation.

[For patients >75 years, NP-guided therapy may not be better than symptom-guided therapy\(^{(25)}\)].

[The BATTLESCARRED study concluded that NT-proBNP-guided treatment was associated with a lower mortality rate (and hospitalization rate) at 3 years compared with either intensive clinical management or usual care for patients <75 years of age].\(^{(24)}\)

[Biologic variability must be considered on the occasion where NPs are measured serially for monitoring and titrating HF treatments. From a study of Irish subjects, it was concluded that changes of approximately 50% and 66% for NT-proBNP and BNP, respectively, are needed to indicate an altered clinical status in stable HF patients\(^{(26)}\)].

[Use of the angiotensin receptor and nepriysin inhibitor (ARNI) Entresto, is reported to cause a modest initial increase in BNP (median BNP: 200 to 250 ng/L) but not NT-proBNP which decreases rapidly during this period. However the magnitude of any such effect of ARNIs on BNP measurement across different BNP assays is currently unknown. Whilst any BNP increase might itself suggest compliance and/or response to treatment, baseline values after one month of treatment should be obtained, whenever monitoring is considered appropriate. Dual use of BNP and NT-proBNP (and with a BNP:NT-proBNP ratio) have been proposed when using ARNIs, to concomitantly monitor progression of HF and provide a comprehensive biological and clinical picture.\(^{(1,12,13)}\) However, until such information is available including data from prospective randomised studies involving ARNIs, we currently recommend NT-proBNP measurements (only) in such patients.]

**Who to Re-Test**

Repeat NP testing is not indicated in the vast majority of inpatients with HF\(^{(3)}\) and should be measured once, with the following exceptions:

1. Primary Care – there is a repeat episode of suspected HF with a change in clinical presentation and the diagnosis of HF has been excluded previously.\(^{(29)}\)
2. Secondary Care (per acute episode) – unless there is clinical deterioration or failure to respond to therapy. It is reasonable to expect such requests to be discussed and justified.

3. Pre-discharge in specified cases (e.g. potential transplant candidates) when the question of prognosis might be of clinical importance, or where the result may impact on follow-up arrangements.

[Pre-discharge repeat measurement has prognostic significance but has not been shown to alter outcome]. (30)

Specimen and Ordering Information

All requests (electronic and paper) and specimens must adhere to the laboratories standard requirements and contain all necessary demographics and should provide the indication for testing and relevant clinical information including date and time of venepuncture, to enable accurate result interpretation. In order to comply with accreditation standards (ISO: 15189:2012), laboratories cannot accept or process samples which do not meet their defined minimum standards.

Specimen pre-requisites for each test are given below:

BNP: EDTA plasma or whole blood (POCT) is the recommended sample type.

[Time between venepuncture and analysis should be minimized particularly for BNP, which shows concentration decreases (mean) of 10% (range: 6-12%) after storage of whole blood for 4 hours (room temperature). After 8 hours under the same conditions, the average decrease is 12% (9-15%) and thereby creating greater potential to confound analysis and generate false negative results. At 4°C, decreases of 5% and 12% are reported for 4 and 8 hours storage, respectively]. (31)

NT-proBNP: Either serum or heparin/EDTA plasma and whole blood (POCT) can be used. [By comparison to BNP, NT-proBNP is more stable, for at least 24 hours storage at room temperature. If resource exists to offer NP analysis to primary care, NT-pro-BNP is the preferred laboratory-based test particularly where pre-analytical delays may be longer (>4h) and unavoidable]. (32)

Laboratories should consult manufacturer’s product specification sheets for their specific BNP/NT-proBNP assay to obtain further information related to sample handling and stability studies.

Decision Cut-off Values, Algorithm for Testing & Confounding Factors

The following tables provide the decision thresholds/cut-off values for BNP and NT-proBNP for ‘ruling-out’ HF. (19,22)

<table>
<thead>
<tr>
<th></th>
<th>BNP cut-off</th>
<th>NT-proBNP cut-off</th>
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<tbody>
<tr>
<td>Non-Acute Setting</td>
<td>&lt; 35 pg/mL</td>
<td>&lt; 125 pg/mL</td>
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<tr>
<td>Acute Setting</td>
<td>&lt; 100 pg/mL</td>
<td>&lt; 300 pg/mL</td>
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</table>

1 The National Institute for Health and Care Excellence (NICE) state that BNP < 100 pg/mL or NTproBNP < 400 pg/mL in an untreated patient make heart failure unlikely. Above these levels,
serum NPs carry poorer prognosis and can be used to guide the selection of patients for transthoracic Doppler 2D echocardiography (ECHO). Elsewhere, a lower threshold (<300 pg/mL) is advocated and shown to improve diagnostic sensitivity. (44)

[In the Breathing Not Properly study involving patients presenting to ED with acute dyspnoea, a BNP cut-off of 100 pg/mL gave the highest sensitivity (90%) and specificity (73%). This study involved the Triage BNP test (Biosite Inc.). (2) Despite methodological differences and bias observed amongst BNP assays, there is comparable ability across BNP (and NT-proBNP) assays to exclude HF (sensitivity, BNP: 95% [95% CI 93-96], NT-proBNP: 99% [95% CI 96-100] using the above cut-offs however specificity is variable. (5)

Rule in cut-offs (36)

<table>
<thead>
<tr>
<th>BNP &gt;500</th>
<th>All Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP:</td>
<td>Age (yrs)</td>
</tr>
<tr>
<td>&gt;450 pg/mL</td>
<td>&lt;50</td>
</tr>
<tr>
<td>&gt;900 pg/mL</td>
<td>50 – 75</td>
</tr>
<tr>
<td>&gt;1800 pg/mL</td>
<td>&gt;75</td>
</tr>
</tbody>
</table>

*At the time of guideline preparation age related thresholds for HF were quoted with the Alere NT-proBNP for Architect assay for patients <75 years (>125 pg/mL) and ≥75 years (>450 pg/mL) respectively.

Defining “rule in” cut-offs for HF is complicated because multiple factors, including age, gender (F>M) and medications influence NP levels (see table below). However, their overall impact is less significant compared with comorbidities such as cardiac, pulmonary and renal disease which are likely to increase NP levels above current thresholds for HF. (1)

[The International Collaborative of NT-proBNP (ICON) study concluded that for diagnosis of HF ("ruling in"), age-dependent cut-points improve the positive predictive value (PPV)]. (37)

Factors affecting NP levels

*Age (↑)
Gender (F>M)
High sodium diet (↑)
Exercise prior to sampling (↑)
Obesity (↓)
Drugs [Diuretics, ACEi, ARBs, Aldosterone Receptor Antagonists, Beta Blockers] (↓)

*Not for all assays. Where observed, effect is greater for BNP vs NT-proBNP in HF patients (vice versa for healthy individuals), though effect of age (and gender) is modest compared to other factors in HF patients. (38)

Lower thresholds should be used to diagnose HF in obese patients. (39) [There is an inverse relationship between obesity and circulating NPs].

Interpreting serial BNP measurements

The large biological variation for NPs must be considered when interpreting serial NP measurements. (26,40) [See above section on Who Not to Test: “Monitoring Treatment for HF”].

Across healthcare regions in Ireland, NP testing has become available to hospital clinicians and in some cases to GPs however audit of its use as a biomarker to rule out HF show a lack of compliance and inappropriate result interpretation by clinical users. (41)
Where NPs are available in the non-acute setting and are elevated, full investigation of precipitating factors and/or alternative diagnoses (e.g. ACS, PE) may be precluded where diagnostic tests for such conditions are not routinely available (e.g. troponin, d-dimers). The use of NPs in this setting is therefore largely limited to ruling out HF, assessing the need for ECHO where NPs are raised and stratified testing as part of collaborative in patients at high risk of HF. Patients with suspected acute HF should therefore be referred immediately for acute care and management.

Algorithms involving the use of NPs in the diagnosis of HF is reported in a number of published guidelines (1,2,13,16) from which we have extracted and synthesised into the following algorithm, encompassing the above diagnostic considerations, to guide appropriate use and interpretation of NPs in the investigation of patients presenting with suspected acute HF.
Patient with suspected HF (typical symptoms):
Assess pre-test probability of HF and exclude non-cardiac cause of dyspnoea by:
*Clinical Evaluation + Diagnostic Investigations

**Typical + specific signs and symptoms which may increase likelihood of HF**
(see also Table 1):

- **Clinical Hx**
  - Hx CAD or arterial HTN, diuretics, breathlessness, orthopnoea/
    paroxysmal nocturnal dyspnoea
- **Physical Exam**
  - Creps, bilateral ankle oedema, jugular venous dilatation, laterally displaced/
    broadened apical beat, Heart murmur
  - ECG
  - Any abnormality

*Obvious clinical diagnosis of AHF (NPs unnecessary for diagnosis)*

Urgently Evaluate + Manage
1. Cardiogenic shock
2. Respiratory failure
3. Precipitating causes

- C: Acute Coronary Syndrome
- H: Hypertension Emergency
- A: Arrhythmia
- M: Mechanical: Acute e.g. trauma, surgery etc.
- P: Pulmonary Disease e.g. PE

Also consider Toxins (alcohol, illicit drugs), Infection (e.g. pneumonia, sepsis), Drugs (↑ salt/fluid retention e.g. steroids, non-compliance or Negative Inotropes e.g. Beta Blockers), Acute cardio/cerebro vascular events and endocrine abnormalities e.g. hyper/hypo thyroid, DKA etc.

**Suspected HF**
≥1 Sign/Symptom (i.e. indeterminate/uncertainty)
*NP*s have greatest diagnostic value in this scenario

Measure NP (BNP or NT-proBNP)
and evaluate against relevant non-acute/acute threshold,
to assess need for ECHO

**No evidence of HF**

HF unlikely: Consider other causes of dyspnoea AND exclude false negatives (Table 2 + 3)

**Cardiac causes of ↑ NP**
(Table 2):
Cardiology +/- ECHO

Confirm and treat non-cardiac causes leading to ventricular stretch and ↑ NP (Table 2)
**Table 1: Signs and Symptoms typical of HF (Ref. 13).**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td></td>
<td><strong>Typical</strong></td>
</tr>
<tr>
<td>Breathlessness</td>
<td>Elevated jugular venous pressure</td>
</tr>
<tr>
<td>Orthopnoea</td>
<td>Hepatogenous reflux</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnoea</td>
<td>Third heart sound (gallop rhythm)</td>
</tr>
<tr>
<td>Reduced exercise tolerance</td>
<td>Laterally displaced apical impulse</td>
</tr>
<tr>
<td>Fatigue, tiredness, increased time to recover post-exercise</td>
<td></td>
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<tr>
<td>Ankle swelling</td>
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<tr>
<td></td>
<td><strong>Less Typical</strong></td>
</tr>
<tr>
<td>Nocturnal cough</td>
<td>Wright gain (&gt;2kg/week)</td>
</tr>
<tr>
<td>Wheezing</td>
<td>Weight Loss (advanced HF)</td>
</tr>
<tr>
<td>Bloating feeling</td>
<td>Tissue wasting (cachexia)</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>Cardiac murmur</td>
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<tr>
<td>Confusion (especially in elderly)</td>
<td>Peripheral oedema (ankle, sacral, scrotal)</td>
</tr>
<tr>
<td>Depression</td>
<td>Pulmonary crepitations</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Reduced air entry and dullness to</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Percussion at lung bases (pleural effusion)</td>
</tr>
<tr>
<td>Syncope</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Irregular pulse</td>
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<tr>
<td>Bendopnea</td>
<td>Tachypnoea</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Cheyne Stokes respiration</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Ascites</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Cold extremeties</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Oliguria</td>
</tr>
<tr>
<td>Bendopnea</td>
<td>Narrow pulse pressure</td>
</tr>
</tbody>
</table>

**Table 2: Cardiac and Non-cardiac causes of elevated natriuretic peptides (Ref. 13)**

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Heart Failure</th>
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<tbody>
<tr>
<td></td>
<td>Acute Coronary Syndromes</td>
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<tr>
<td></td>
<td>Myocarditis</td>
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<tr>
<td></td>
<td>Left Ventricular Hypertrophy</td>
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<td></td>
<td>Hypertrophic or restrictive cardiomyopathy</td>
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<tr>
<td></td>
<td>Valvular heart disease</td>
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<tr>
<td></td>
<td>Congenital heart disease</td>
</tr>
<tr>
<td></td>
<td>Arterial and ventricular tachyarrhythmias</td>
</tr>
<tr>
<td></td>
<td>Heart conduction</td>
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<tr>
<td></td>
<td>Cardioversion, ICD shock</td>
</tr>
<tr>
<td></td>
<td>Surgical procedures involving the heart</td>
</tr>
<tr>
<td></td>
<td>Pulmonary hypertension</td>
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<table>
<thead>
<tr>
<th>Non-cardiac</th>
<th>Advanced age</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Ischaemic stroke</td>
</tr>
<tr>
<td></td>
<td>Subarachnoid haemorrhage</td>
</tr>
<tr>
<td></td>
<td>Renal dysfunction</td>
</tr>
<tr>
<td></td>
<td>Liver dysfunction (mainly liver cirrhosis with ascites)</td>
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<tr>
<td></td>
<td>Paraneoplastic syndrome</td>
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<tr>
<td></td>
<td>Chronic obstructive pulmonary disease</td>
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<tr>
<td></td>
<td>Severe infections (including pneumonia and sepsis)</td>
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<tr>
<td></td>
<td>Severe burns</td>
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<tr>
<td></td>
<td>Anaemia</td>
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<tr>
<td></td>
<td>Severe metabolic and hormone abnormalities</td>
</tr>
</tbody>
</table>

**Table 3: Causes of Falsely Low Natriuretic Peptides**

<table>
<thead>
<tr>
<th>False negative: Low B-type natriuretic peptide with heart failure</th>
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</thead>
<tbody>
<tr>
<td>Failure to adjust cut-off values for:</td>
</tr>
<tr>
<td>- Age</td>
</tr>
<tr>
<td>- Gender</td>
</tr>
<tr>
<td>Flash pulmonary oedema</td>
</tr>
<tr>
<td>Acute mitral regurgitation</td>
</tr>
<tr>
<td>Mitral stenosis</td>
</tr>
<tr>
<td>Atrial myxoma</td>
</tr>
<tr>
<td>Fully treated low-grade heart failure</td>
</tr>
</tbody>
</table>

**Note:** Low BNP may also be seen in patients with obesity, right-sided AHF or decompensated end-stage HF.
Recommendations for National Laboratory Information System (MedLIS)

An order entry form has been developed to facilitate test ordering in line with this national guideline, agreed with the National Clinical Programme for Heart Failure as follows:

**Order Entry form for GPs:** Clinical details field – mandatory free text field.

Indication for testing – drop down menu:

- Possible new HF
- Deterioration ?cause
- Discussed with Lab.

**Order entry form for in-patients:** Clinical details field – mandatory free text field.

Indication for testing – drop down menu:

- Cardiac Admission
- Discharge
- Other (specify).

**Heart Failure Annual Review Care Set:**

FBC – ticked

U&E – ticked

BNP or NT-proBNP – unticked.

Rule to be built: If care set ordered within the last 11 months pop-up to state “This care set cannot be ordered within 11 months of previous annual review”.

A suite of interpretive comments will be developed with the National Clinical Programme for Heart Failure.

**Information for Patients**

There is no special patient preparation required prior to blood testing for BNP or NT-proBNP. NPs are not affected by posture or circadian rhythm and therefore timing of appointments for venepuncture is not as important as it might be for other tests e.g. testosterone. (42,43)

BNP or NT-proBNP testing assists the general practitioner or hospital physician to diagnose, monitor and risk stratify patients with either known or suspected HF.

BNP or NT-proBNP may be used along with a chest x-ray, ECG, and Doppler echocardiography in the clinical assessment for suspected HF both in outpatient and in the emergency care settings.
Guideline Development Methodology - Consultation Plan and History

The guideline was drafted by the authors, followed by expert consultation with the National Clinical Programme for Heart Failure. Following incorporation of feedback the guideline was submitted to the full National Clinical Programme for Pathology consultation process.

Acknowledgements

We acknowledge Prof Niall Mahon (Consultant Cardiologist/Clinical Professor of Medicine, Department of Cardiology, MMUH and UCD) for his advice and comment during the preparation of this guideline.

References


Appendix: Quick Reference Card

- Testing for Natriuretic Peptides (NPs) involves the analysis of either BNP (EDTA plasma) or NT-proBNP (serum or plasma), by the central laboratory or through point of care testing (POCT, whole blood). NPs are most useful in supporting the diagnosis of ambulatory and acute decompensated heart failure (HF), especially in the setting of clinical uncertainty.

- There is currently no difference in diagnostic and prognostic performance between BNP and NT-proBNP. Central laboratory and POCT testing show comparable performance.

- BNP and NT-proBNP test results are not interchangeable and cannot be directly compared.

**Indications for NP testing:**

- Differential diagnosis of dyspnoea in patients of suspected HF, especially when echocardiography is not immediately available. NPs should be used and interpreted along with clinical assessment (including confounding factors), ECG, chest X-ray and echocardiography. A single measurement is adequate for ‘rule out’.

- Risk stratification and prognosis (in-patients), on admission + prior to discharge.

- Screening for HF in high risk populations (e.g. post MI, diabetes, hypertension).

These indications are in line with the National Heart Failure Programme:

<table>
<thead>
<tr>
<th>NP testing in Primary Care:</th>
</tr>
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<tbody>
<tr>
<td>&gt;Possible new onset of HF (Diagnostic aid)</td>
</tr>
<tr>
<td>&gt;Patient deteriorating where HF is part of the differential (unless clear clinical cardiac or respiratory cause)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NP testing in the Hospital setting:</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;Emergency admission with breathlessness, likely of cardiac origin (Diagnostic+Prognostic value)</td>
</tr>
<tr>
<td>&gt;At discharge following treatment for HF (Prognostic value)</td>
</tr>
<tr>
<td>&gt;Deterioration or failure to respond to treatment during admission (Justification required)</td>
</tr>
</tbody>
</table>

**Circumstances where NP testing is not recommended:**

- Patients with classic signs of acute decompensated HF or those with shortness of breath consistent with other aetiologies.

- Screening for asymptomatic ventricular dysfunction.

- Widespread monitoring of treatment for HF.

- Daily monitoring of NP is inappropriate.

*Refer to the full guideline for Decision Thresholds and Algorithm for guiding appropriate Use and Interpretation of NPs in the Investigation of patients presenting with suspected HF.*