



BNP AND CONGESTIVE HEART FAILURE

Heart failure is a major health problem and is the most frequent cause of hospitalization for patients > 65 years of age. In this age group, prevalence is > 10% and only 50% of patients survive 5 years. More than 15 million patients in North American and Europe have heart failure with more than 1.5 million new cases per year.¹ Accurate diagnosis is often difficult as the clinical signs and symptoms of heart failure are neither sensitive nor specific and overlap considerably with pulmonary disease.

The release of B-type natriuretic peptides (BNP) by cardiac myocytes in response to ventricular stretching renders BNP useful in the assessment of heart failure and left ventricular function.

Biosynthesis and Metabolism

BNP is an active hormone, synthesized by the cardiac myocyte as a pre-pro-hormone of 134 amino acids. The precursor hormone is split into two proteins by plasma proteases, the physiologically active C-terminal-BNP and the inactive N-terminal pro-hormone fragment and is then released into the bloodstream. Both fragments appear at increased concentrations in patients with congestive heart failure (CHF).

The natriuretic peptides regulate blood pressure, electrolyte balance and fluid volumes. BNP binds to natriuretic peptide receptors on the vascular endothelium and renal parenchyma cells and decreases blood pressure and blood volume overload by stimulating excretion of sodium and water. BNP levels correlate well with ventricular functional status and hence have been shown to be a clinically useful assay.

Clinical Utility

A linear relationship can be observed between increasing BNP and severity of heart failure. BNP has an excellent predictive value for diagnosis of CHF in patients who present with shortness of breath and chest pain. A BNP concentration > 100 pg/mL is a strong independent predictor of CHF with 90% sensitivity and 76% specificity.² Survival rates inversely correlate with BNP levels. Wang *et. al.* have recently noted that at concentrations of > 80 pg/mL, an increasing level of BNP is a predictor of a first cardiovascular event, heart failure and atrial fibrillation and even stroke in asymptomatic patients.³

BNP Clinical Utility

- Elimination of CHF as a reason for dyspnea
- Diagnosis of early CHF
- Staging of CHF
- Prognosis and risk stratification of CHF
- Predicting outcomes after AMI

BNP has been shown to be helpful in risk stratification as approximately 60% of patients with Class I CHF have nonspecific clinical or echoradiography results, but have elevated concentrations of BNP.

Serial measurements may also be an effective way to improve the management of patients, monitoring response to therapy and prognosis at discharge. Currently, the BNP assay is not FDA approved for monitoring of the drug nesiritide used to treat CHF, as the assay will detect both endogenous and exogenous forms of BNP.⁴ However, it may be possible to monitor nesiritide BNP therapy using pro-BNP

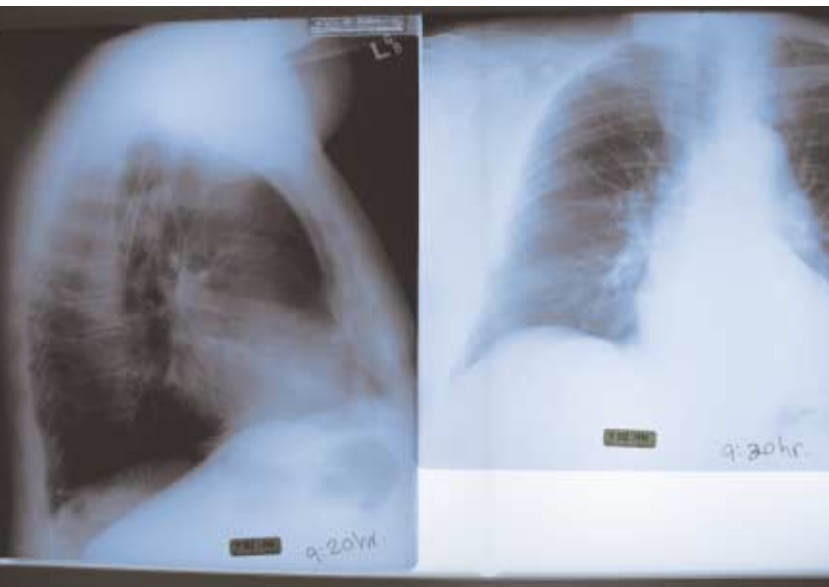
Result Interferences

BNP is not influenced by, diabetes, hypertension or chronic obstructive pulmonary disease. BNP is however, increased in renal failure and cirrhosis. Concentrations increase with age and are higher in women than men, but age and sex adjusted cutoff values have not been established.⁵

Non-cardiac conditions with elevated BNP

- Renal Failure
- Cirrhosis
- Age
- Primary pulmonary hypertension
- Endocrine disease i.e. primary hyperaldosteronism and Cushing syndrome

Serum BNP Concentration	Interpretation
< 100 pg/mL	95% Negative predictive value for CHF
100-500 pg/mL	Increasing probability of CHF
> 500 pg/mL	CHF highly likely



Test Availability

MDS is currently offering analysis of total BNP and the physiologically active derivative. Careful collection and sample handling is important to ensure validity of results. Blood should be collected in plastic EDTA tubes. Samples should be centrifuged and promptly separated. BNP is stable for 4 hours at room temperature or 24 hours at 4C and must be frozen if stored for longer periods.

Results of this assay are not interchangeable with data from measurement of NT pro-BNP.

The test is not covered by OHIP at this time, however it may be covered by the patient's extended health plan. ■



REFERENCES

1. McCullough PA et. al. J Am Coll Cardiol. 2002; 39: 60-69 .
2. Maisel AS et. al. N Eng J Med. 2002: 347; 161-167.
3. Wang TJ et. al. N Engl. J. Med. 2004: 350; 655-663.
4. Wu et. al. Clin. Chem. 2004: 50: 867-873.
5. Redfield, MM, J, Am Coll Cardiol. 2002: 40: 976-982.

LYMPHOCYTE MARKER ANALYSIS (USING FLOW CYTOMETRY)

The "Lymphocyte Marker Analysis Form" requires that you indicate the suspected diagnosis or reason for ordering the test. Please do not state "Lymphocyte Markers" or "Flow cytometry" as the suspected diagnosis or reason for ordering the test, as this does not provide the specific information necessary for the selection of markers to be tested by the laboratory.

If the specimen is collected in your office, it is also necessary to provide the date and time of sample collection.

Specimens or requests submitted without the required information cannot be processed and will be rejected.

The "Lymphocyte Marker Analysis Form" is available by calling the MDS Customer Care Centre at 416-675-3637, or 1-877-849-3637, and is also available in the Directory of Laboratory Services. ■

BETA-2 MICROGLOBULIN

On April 4th, MDS implemented nephelometric evaluation of serum beta-2 microglobulin. Elevated concentrations of serum beta-2 microglobulin may be related to increased activity of the immune system or decreased elimination associated with renal damage. Serum beta-2 microglobulin is a sensitive marker for the glomerular filtration capacity of the kidneys and is a good prognostic marker in multiple myeloma. ■

TESTOSTERONE

MDS utilizes the Immulite 2000 for quantitation of total serum testosterone. As a result of a recent re-standardization of this assay by the manufacturer, total testosterone results may be expected to decrease by about 20% across the analytical range. The reference intervals for both males and females have been updated to reflect this change to testosterone results. ■

THYROGLOBULIN

On March 7th, MDS initiated testing of thyroglobulin using the Immulite 2000 chemiluminescent technology. Thyroglobulin is useful in the differential diagnosis of congenital hypothyroidism and may also be of value in distinguishing between subacute thyroiditis and thyrotoxicosis. It is useful in the management of differentiated thyroid carcinomas. Thyroglobulin results should always be interpreted in combination with anti-thyroglobulin antibody results. The presence of these circulating antibodies may cause underestimation of the thyroglobulin result, as measured by this assay. ■