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ROCHE ELECSYS® PROBNP ASSAY PROVIDES RISK ASSESSMENT OF CARDIAC EVENTS FOR PEOPLE WITH STABLE CORONARY ARTERY DISEASE

The FDA has recently cleared the **Roche Elecsys® proBNP Assay** for new risk stratification use. The test may also now serve as an aid in the assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease. The test is currently FDA-approved as an aid in the diagnosis of individuals suspected of having congestive heart failure and is further indicated for the risk stratification of patients with acute coronary syndrome and congestive heart failure.

ProBNP is secreted mainly by the left ventricle of the heart when the heart is unable to pump blood efficiently, in response to volume expansion in the peripheral circulation, pressure overload, or increased wall tension. During the process of secretion, it is cleaved to yield the active hormone, brain natriuretic peptide (BNP), and the N-terminal fragment, NT-proBNP, which is biologically inactive. In subjects with left ventricular dysfunction, serum and plasma concentrations of NT-proBNP have been shown to be increased. A high amount of NT-proBNP in the blood indicates the presence of ventricular remodeling. The higher the blood level of NT-proBNP, the more serious is the condition.

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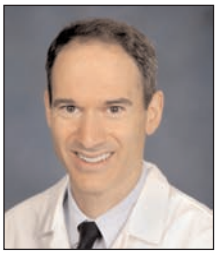
Nearly 13 million Americans have stable coronary artery disease, and people with this condition are at a higher risk of developing adverse cardiac events than the general population. Because primary care providers are usually the first line of defense in treating patients with stable coronary artery disease, the NT-proBNP assays would have particular value aiding in the assessment of these patients. As a reliable indicator of cardiac involvement in the disease process, this test can facilitate identification of patients who are at increased risk, allowing physicians to differentiate disease states and individualize therapy, or refer suspected high risk cases back the cardiologist for further evaluation and treatment.



Christopher R. deFilippi, MD; FACC, Associate Professor of Medicine, University of Maryland School of Medicine, Division of Cardiology (Baltimore, MD) says that by having this new indication, this is not just a heart-failure specific test. “What we're recognizing is that levels of NT-proBNP can be elevated for reasons other than developing heart failure. It's a test where you can prognosticate very well in individuals who have chronic ischemic heart disease. It appears that ischemia by itself, in the absence of any heart failure findings, can drive up the level and the higher the level, the poorer the prognosis. The message you can draw from this is that if you find an elevated level but you ultimately decide that the patient doesn't have heart failure, you still know they have underlying ischemic heart disease and this level is of significance in terms of prognosis.” Dr. deFilippi goes on to say, “you can think of natriuretic peptides as cardiac distress hormones—a variety of cardiac related problems can lead to an elevation. Ultimately, the onus is on the physician to decide what the underlying cardiac

problem is, but if you have an elevated level, you should know that you do have a related problem—it's not a result of something that's not cardiac. I think that's a lot of the power in it."

David A. Morrow, MD, MPH, TIMI Study Group, Cardiovascular Division, Brigham & Women's Hospital (Boston, MA), says that, "natriuretic peptides have had tremendous evolution in clinical application. The NT-proBNP marker started with a fairly narrow diagnostic application in patients presenting with shortness of breath where it was found to be very useful in identifying patients with heart failure as opposed to non-cardiac causes of shortness of breath. Through our research we have found both NT-proBNP and BNP to be very robust markers of prognosis that factor among the strongest predictive markers that we have for the risk of death or heart failure when a patient comes in with a heart attack or unstable angina. We now know that levels of NT-proBNP also give us a lot of information with respect to prognosis for these patients. These patients are not presenting at the hospital with a heart attack, but they might be seen in the clinic with angina or following a heart attack once they are well stabilized. This biomarker can be valuable, along with the history and clinical exam, in its prediction of future cardiovascular events for these patients as well. We need to identify therapies that lower the risk associated with increased natriuretic peptides in order to translate the prognostic findings toward maximal clinical utility."

A recent study assessed the relationship between NT-proBNP levels and long-term mortality from all causes in a large group of patients with stable coronary disease. Baseline serum samples of NT-proBNP were measured in 1034 patients referred for angiography related to signs or symptoms of coronary heart disease. The rate of death from all causes was determined after a median follow-up of nine years. The study concluded that NT-proBNP is a marker of long-term mortality in patients with stable coronary disease and provides prognostic information beyond that provided by conventional cardiovascular risk factors and the degree of left ventricular systolic dysfunction. At follow-up, 288 patients had died. The median NT-pro-BNP level was significantly lower among patients who survived than among patients who died. (120 pg per milliliter [interquartile range, 50 to 318] vs. 386 pg per milliliter [interquartile range, 146-897], $P<0.001$). Patients with NT-pro-BNP levels in the highest quartile were older, had a lower left ventricular ejection fraction and a lower creatinine clearance rate, and were more likely to have a history of myocardial infarction, clinically significant coronary artery disease, and diabetes than patients with NT-pro-BNP levels in the lowest quartile. In a multivariable Cox regression model, the hazard ratio for death from any cause for the patients with NT-pro-BNP levels in the fourth quartile as compared with those in the first quartile was 2.4 (95 percent confidence interval, 1.5 to 4.0; $P<0.001$).

Roche Diagnostics has recently moved to the number one position worldwide in the cardiac marker market, and proBNP is the only natriuretic peptide test that is approved in the U.S. for cardiac risk stratification in people with stable coronary artery disease.

For more information concerning the Roche Elecsys® proBNP Assay or other products, call 1-800-428-5074, or visit the company's Web site at www.roche-diagnostics.us.