

Galectin-3, a Novel Biomarker for Additional Heart Failure Risk Stratification

Introduction

Heart failure (HF) is a multifaceted syndrome characterized by many potential etiologies, diverse presentations, and many clinical subsets. As HF progresses, symptom severity may vary and may not reflect precursory changes in underlying cardiac function.¹ Principal manifestations include dyspnea and fatigue, which may impact tolerance for physical activity, and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral edema.² Lacking a single test that can accurately diagnose HF, physicians typically base their diagnoses of HF on the results of a thorough history and physical examination.²

An Emerging Biomarker for Risk Stratification

According to the 2013 practice guideline on heart failure management from the American College of Cardiology Foundation and the American Heart Association, routine evaluation of HF patients should include an assessment of the potential for adverse outcomes, because risk stratification may help inform management decisions, including accelerated transition into advanced therapies.² Further, the guideline recognizes galectin-3 as an emerging biomarker of myocardial fibrosis that is predictive of hospitalization and death, as well as additive to the prognostic value of the natriuretic peptides (NP) in HF patients.²

Galectin-3 Clinical Studies and Results Interpretation

In an evaluation of chronic HF patients who participated in the Deventer-Alkmaar heart failure study (DEAL-HF), 49% had elevated levels of galectin-3 (≥ 17.8 ng/mL).³

Galectin-3 levels were assessed in samples from 895 of the 2,331 chronic HF patients who participated in the Heart Failure: a Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) study. Key points from this evaluation included the following⁴:

- The 895 patients had left ventricular dysfunction and symptoms that fell within New York Heart Association (NYHA) classes II, III, or IV.
 - The average age of patients was 58 years; 29% were female, and 36% were nonwhite.
 - Median follow-up was approximately 30 months. Primary end points were all-cause mortality and hospitalization and cardiovascular mortality.
- Patients were stratified into 3 groups based on their galectin-3 levels:
 - ≤ 17.8 ng/mL
 - >17.8 ng/mL – ≤ 25.9 ng/mL
 - > 25.9 ng/mL
 - Patients with galectin-3 levels greater than 17.8 ng/mL were found to have a higher risk of mortality and/or hospitalization compared to patients with levels below 17.8 ng/mL.

Table 1 shows hazard ratios for these patients, comparing patients with galectin-3 levels ≤ 17.8 ng/mL to those with levels >17.8 ng/mL to ≤ 25.9 ng/mL and to those with levels >25.9 ng/mL).

Table 1: Hazard Ratios for Cardiovascular Mortality Events for HF Subjects in the Clinical Evaluation Study⁴

Galectin-3 Level (ng/mL)	Hazard Ratio for All-cause Hospitalization and Death	Hazard Ratio for Cardiovascular Death
>25.9	1.46	2.33
$>17.8-25.9$	1.35	1.91

Note that galectin-3 levels between 17.8 ng/mL and 25.9 ng/mL should be interpreted with caution, because these values lie within the reference interval.⁴

Galectin-3 and Natriuretic Peptides (BNP or NT-proBNP) in the Outpatient/Ambulatory Setting

Increasingly, clinicians have come to rely on natriuretic peptides (NP) values to confirm a diagnosis of HF and establish its severity. NP levels have become particularly important when the etiology of dyspnea is unclear in ambulatory HF patients or those with acute decompensated HF. However, it is important to note that while lower NP values generally rule out HF and higher values are strongly positive for the presence of disease, elevated NP values have also been associated with the cardiac and noncardiac causes listed on page 2.²

Clinicians are beginning to incorporate galectin-3 into inpatient and outpatient settings to gain additional information that may assist them in the overall risk management of their HF patients.

It has been reported that NP values in the “mid-range,” in which many HF patients fall, are less helpful in diagnosing HF than values at the low and high ranges.⁵ Given the lack of specificity for these patients, and because the clinical utility of serial NP measurement in the reduction of hospitalizations or death has not been well established, combining galectin-3 with either of the natriuretic peptides NP may enhance risk stratification in patients with chronic HF.²

Table 2 shows the 6-month event rates from the clinical validation study for the composite endpoint of all-cause mortality and all-cause hospitalization using marker combinations of galectin-3 and NT-proBNP.

Table 2: Six-month Event Rates for the Composite End-point of All-Cause Mortality and All-Cause Hospitalization by Galectin-3 Category and NT-proBNP Level for HF Subjects in the Clinical Validation Study⁴

Galectin-3* and NT-proBNP** Levels	Event Rate at 6 Months
Neither elevated	19.4%
Any 1 marker elevated	31.8%
Both elevated	42.7%

* Elevated galectin-3: >17.8 ng/m
 ** Median NT-proBNP level: 848 pg/mL

Selected Causes of Elevated Natriuretic Peptide Concentrations²

Cardiac	Noncardiac
Heart failure, including RV syndromes	Advancing age
Acute coronary syndrome	Anemia
Heart muscle disease, including LVH	Renal failure
Valvular heart disease	Pulmonary: obstructive sleep apnea; severe pneumonia, pulmonary hypertension
Pericardial disease	Critical illness
Atrial fibrillation	Bacterial sepsis
Myocarditis	Severe burns
Cardiac surgery	Toxic-metabolic insults, including cancer chemotherapy and envenomation
Cardioversion	

Test Name	Test N°	Relevant Assays	Test N°
Galectin-3	004110	Galectin-3 with NT-proBNP	142005
		NT-proBNP	143000

Visit the online Test Menu at www.LabCorp.com for full test information, including CPT codes and specimen collection requirements.

References

- Heart Failure Society of America, Lindenfeld J, Albert NM, Boehmer JP, et al. Executive Summary: HFSA 2010 Comprehensive Heart Failure Practice Guideline. *J Card Fail.* 2010;16(6):475-539.
- Yancy CW, Jessup M, Bivkem B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A report of the American College of Cardiology Foundation/American heart Association Task Force on Practice Guidelines. *Circ.* 2013;128:1-115.
- Lok DJA, van der Meer P, de la Porte PWB, et al. Prognostic value of galectin-3, a novel marker of fibrosis, in patients with chronic heart failure: Data from the DEAL-HF study. *Clin Res Cardiol.* 2010; 99(5):323-328.
- BGM Galectin-3™ [package insert]. Waltham, MA: BG Medicine Inc.;2010.
- Titus K. Heart Failure high-wire act. *CAP Today.* July 2013. http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtl_t_actionOverride=%2Fportlets%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtl&cntvwrPtl%7BactionForm.contentReference%7D=cap_today%2F0713%2Fheart_failure.html&_state=maximized&_pageLabel=cntvwr. Accessed July 30, 2013.

