Circ J 2004; Tanaguchi R et al. *Heart Vessels* 2006]. Yukihito Sato, MD, Amagasaki Hospital, Hyogo, Japan, discussed the association between TnT and prognosis in patients with HF.

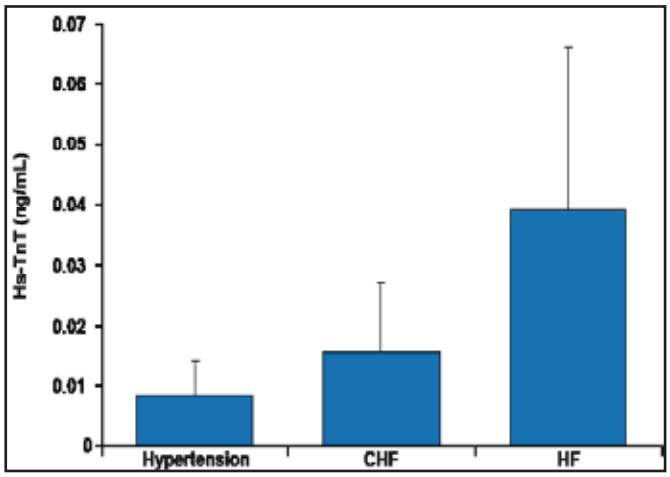
High-sensitivity TnT (hs-TnT) assays accurately measure very low TnT concentrations. The Val-HeFT study found an association between high levels of hs-TnT and HF mortality and hospitalizations [Latini R et al. *Circulation* 2007].

In patients with acute decompensated HF, those with the highest baseline TnT or troponin I (TnI) had the highest risk of in-hospital mortality [Peacock WF 4th et al. *N Engl J Med* 2008]. Dr. Sato showed that elevated baseline hs-TnI in patients with acute HF was associated with a higher rate of cardiac events ($p<0.05$) [Kuwabara Y et al. *Circ J* 2007]. In another study, acute HF patients with elevated serial hs-TnI had the highest rate of cardiac events versus those with low serial hs-TnI [Xue Y et al. *Eur J Heart Fail* 2011].

Hs-TnT has been detected in 80% of patients with essential hypertension [Sato Y et al. *J Cardiol* 2011] and in 66% of community-dwelling older adults [deFilippi CR et al. *JAMA* 2010]. The baseline concentration of hs-TnT and a >50% increase in hs-TnT at follow-up in the community-dwelling population were predictors of adverse CV events.

Concentrations of hs-TnT increase with the severity of heart disease, from hypertension to CHF to acute HF (Figure 1). Dr. Sato concluded that baseline TnT concentration and elevated serial TnT concentrations at follow-up are prognostic markers in patients with HF. Combined measurements of TnT and BNP can identify patients at highest risk of adverse cardiac events. Patients with the highest hs-TnT concentrations have the highest risk of adverse cardiac events.

Figure 1. Concentrations of hs-TnT in Hypertension, CHF, and Acute HF.



CHF=chronic heart failure; HF=heart failure; hs-TnT=high-sensitivity troponin T.
Reproduced with permission from Y. Sato, MD.

Risk Prediction in Chronic Heart Failure

Studies have suggested using a panel of biomarkers that measure diverse biological processes as a prognostic tool for heart failure (HF). Thomas P. Cappola, MD, ScM, University of Pennsylvania, Philadelphia, Pennsylvania, USA, presented the Penn Heart Failure Study based on the hypothesis that multiple biomarkers considered together are superior to clinical risk stratification in patients with chronic HF [Ky B et al. *Circ Heart Fail* 2012]. The aim of the study was to derive a biomarker score in ambulatory HF patients that predicts time to transplant, left ventricular assist device (LVAD), or death and to compare its performance to the Seattle Heart Failure Model (SHFM).

A total of 1513 patients with HF were evaluated with biomarker analysis on banked serum, plasma, and DNA; 2D echocardiogram; and detailed clinical covariates (SHFM). Eight candidate biomarkers that measure distinct biological processes and are individually associated with adverse outcomes were evaluated using high-quality assays: troponin I (TnI) for myocyte injury, creatinine for renal function, soluble toll-like receptor-2 (ST2) for myocyte stress, soluble fms-like tyrosine kinase receptor-1 (sFlt-1) for vascular remodeling, B-type natriuretic peptide (BNP) for neurohormones, myeloperoxidase and uric acid for oxidative stress, and high-sensitivity C-reactive protein (hsCRP) for inflammation.

At a median 2.5 years follow-up, 317 events had been reported, including 31 LVADs, 99 transplants, and 187 deaths. After biomarker evaluation using multiple methods, 7 markers remained in the multimarker score: BNP, sFlt-1, hsCRP, ST2, TnI, uric acid, and creatinine. The multimarker score was a strong predictor of adverse outcomes. The hazard ratio for adverse outcomes was 4.7 in patients with a moderate multimarker score and 15 in patients with a high multimarker score. The multimarker score was a stronger predictor of adverse outcomes than the SHFM score (AUC, 0.798; 95% CI, 0.763 to 0.833; $p<0.01$). Adding the multimarker score to the SHFM led to a significantly improved AUC of 0.803 (95% CI, 0.769 to 0.837; $p<0.01$). After SHFM risk stratification, the multimarker score improved risk assignment in 20% of patients (95% CI, 4.8% to 35.1%; $p=0.01$).

The derived multimarker score comprised of 7 biomarkers is an accurate predictor of adverse outcomes and has improved predictive accuracy compared to a clinical risk score. The same results were obtained using multiple analytic approaches. Broader screens using unbiased technologies are needed, as are clinical trials to prove the utility of biomarkers for risk prediction.