death, myocardial infarction (MI), ischemia-driven revascularization, and stent thrombosis in patients undergoing percutaneous coronary intervention (PCI) with no excess in severe bleeding compared with clopidogrel loading at the time of PCI.

The Clinical Trial Comparing Cangrelor to Clopidogrel Standard Therapy in Subjects Who Require Percutaneous Coronary Intervention [CHAMPION PHOENIX; Bhatt DL et al. *N Engl J Med* 2013] followed 2 prior studies of cangrelor, CHAMPION PLATFORM [Bhatt DL et al. *N Engl J Med* 2009] and CHAMPION PCI [Harrington RE et al. *N Engl J Med* 2009], 2 large Phase 3 trials that had been stopped early when an interim analysis concluded that the trials were unlikely to show that cangrelor was superior to clopidogrel. Deepak L. Bhatt, MD, MPH, Harvard Medical School, Boston, Massachusetts, USA, presented the results of the CHAMPION PHOENIX study in a late-breaking clinical trial.

Cangrelor is a rapidly acting (half-life of 3 to 6 minutes), reversible and intravenous ADP receptor antagonist that permits return to normal platelet function within one hour after discontinuation. These characteristics have spurred interest in its use in the setting of PCI. The CHAMPION PHOENIX trial was a randomized, double-blind, double-dummy, superiority study conducted globally at 153 sites in 12 countries [Bhatt DL et al. *N Engl J Med* 2013]. The primary efficacy endpoint was the composite of death, MI, ischemia-driven revascularization, and stent thrombosis at 48 hours. Secondary endpoints included the incidence of stent thrombosis at 48 hours, and efficacy endpoints were examined at 30 days. The primary safety endpoint was GUSTO severe bleeding at 48 hours.

Patients with stable angina, non-ST-elevation acute coronary syndrome or ST-elevation MI (STEMI; n=10,900) requiring PCI who were included in the study. Eligible patients could not have received pretreatment with a P2Y12 inhibitor prior to angiography or at any time within 7 days prior to randomization. Once suitability for PCI was confirmed by either angiography or STEMI diagnosis, patients were randomly assigned to 2 arms: Group A received a cangrelor bolus and infusion (30 µg/kg, 4 µg/kg/min) and placebo clopidogrel for the duration of the procedure with a minimum duration of 2 hours and a maximum duration of 4 hours, then clopidogrel 600 mg after the end of the infusion; Group B received placebo bolus and infusion along with active clopidogrel with the loading dose chosen by the investigator (300 or 600 mg) [Bhatt DL et al. *N Engl J Med* 2013].

The study population had a median age of 64 years, were mostly male (72%), the majority were enrolled with stable angina (56%), and most (74%) received a 600-mg loading dose of clopidogrel [Bhatt DL et al. *N Engl J Med* 2013]. Treatment with cangrelor significantly reduced the primary endpoint compared with clopidogrel (4.7% vs 5.9%; OR, 0.78; 95% CI, 0.66 to 0.93; p=0.005).

There was no difference with respect to mortality or for ischemia-driven revascularization, but MI was significantly less frequent with cangrelor (3.8% vs 4.7%; OR, 0.80; 95% CI, 0.67 to 0.97; p=0.02). Subgroup analyses showed consistency of benefit with no significant heterogeneity, with the exception of patients with peripheral artery disease (n=832; p for interaction=0.003) in whom cangrelor appeared to have a nominally more robust benefit. Efficacy results were similar when extended out to 30 days. There were no significant excess in GUSTO severe bleeding (0.16% vs 0.11%; OR, 1.5; 95% CI, 0.53 to 4.22; p=0.44) or transfusions (p=0.16); however, there was more ACUITY major bleeding (4.3 vs 2.5; OR, 1.72; 95% CI, 1.39 to 2.13; p<0.001) with cangrelor compared with clopidogrel. Transient dyspnea occurred more frequently in the cangrelor group (1.2% vs 0.3%; p<0.001).

Limitations of this study include the use of a 300-mg clopidogrel loading dose in 1405 patients in the comparator arm (although results were consistent after adjustment for loading dose), the use of clopidogrel as the comparator instead of the more rapidly acting and potent later generation agents prasugrel and ticagrelor, and the exclusion of patients who were pretreated with clopidogrel prior to angiography. No economic analyses have been presented to-date, and this will remain an important consideration should cangrelor become available for clinical use.

Although patients pretreated with ADP receptor blockers were excluded, the findings support a strategy where treatment with potent anti-platelet therapy may not be necessary prior to delineation of coronary anatomy, which may be beneficial for patients subsequently determined to need urgent surgery. In addition, this intravenous therapy presents an option for patients unable to take oral medications. Dr. Bhatt concluded that intravenous cangrelor might offer an attractive option across the full spectrum of PCI, including stable angina, non-STEMI, and STEMI.

BNP Screening, Targeted Care Reduce Heart Failure in At-Risk Patients

Written by Wayne Kuznar

Structured screening for heart failure (HF) using measurement of B-type natriuretic peptide (BNP) followed by targeted collaborative care was effective at preventing left ventricular dysfunction (LVD) and HF in a community setting.

Using clinical criteria alone to identify patients who may be at risk for HF and instituting preventive therapy has been shown to be of relatively limited value. The use of biomarkers related to ventricular damage or dysfunction may improve the ability to identify individuals at risk and ultimately prevent downstream complications. Because it reflects established cardiovascular (CV) insult rather than CV risk, BNP might help identify high risk patients and help focus care where it is needed most, said Kenneth McDonald, MD, Heart Failure Unit, St. Vincent's University Hospital, Dublin, Ireland, in providing the rationale for the St. Vincent's Screening to Prevent Heart Failure study [STOP-HF; NCT00921960].

STOP-HF was conducted in 39 collaborating primary-care practices referring into one CV center in Dublin, and enrolled asymptomatic patients aged >40 years with at least one risk factor for HF (such as hypertension, hyperlipidemia, diabetes, vascular disease, arrhythmia, and obesity).

Of the 1374 patients randomized, those in the intervention group (n=697) were screened annually with BNP measurement and underwent echocardiography and other tests in consultation with a cardiologist if the BNP was >50 pg/mL, while those in the control group (n=677) received standard care from their primary physicians (Table 1). The primary endpoint was the prevalence and severity of LVD (defined as left ventricular ejection fraction <50% [systolic] or E/e prime >15 [diastolic] and measured by Doppler echocardiography). The secondary endpoint was incidence of major adverse cardiac events (MACE), defined as HF, arrhythmia, myocardial infarction, unstable angina, cerebrovascular event, transient ischemic attack, pulmonary embolism, or peripheral thrombosis.

Table 1. STOP-HF Intervention and Routine Care

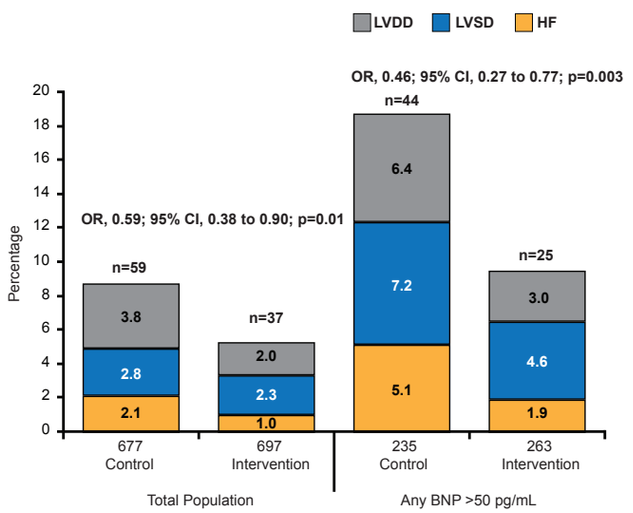
Routine PCP Care	NP-Directed Care
▪ Annual BNP not available to clinicians	▪ Annual BNP in all (in addition to routine PCP care)
▪ At least annual review by PCP ▪ Cardiology review only if requested by PCP	▪ Shared-care (if BNP>pg/mL at any time) » Cardiology review » Echo-Doppler » Other CV investigations » CV nurse coaching » Regular cardiology follow-up

BNP=B-type natriuretic peptide; CV=cardiovascular; PCP=primary-care physician.

About one fourth of the patients in each group had 3 or more risk factors for HF, with hypertension the most prevalent, present in ~60% in each group. The mean BNP was 47 pg/mL and mean systolic blood pressure was 146 mm Hg.

After a mean follow-up of 4.2 years, the odds of achieving the primary endpoint were 41% lower in the intervention group compared with the control group (5.3% vs 8.7%; OR, 0.59; 95% CI, 0.38 to 0.90; p=0.01; Figure 1). The reduction in risk in the intervention group was driven primarily by a 54% reduction in the rate of primary endpoint episodes in patients with any BNP level >50 pg/mL (9.5% in the intervention group vs 18.7% in the control group; 0.46; 95% CI, 0.27 to 0.77; p=0.003; Figure 1).

Figure 1. Components of Primary Endpoint



BNP=B-type natriuretic peptide; HF=heart failure; LVDD=left ventricular diastolic dysfunction; LVSD=left ventricular systolic dysfunction.

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The secondary endpoint of MACE was reduced by 33% in the intervention group relative to controls (OR, 0.66; 95% CI, 0.46 to 0.98; p=0.04). In the subgroup of patients with BNP >50 pg/mL, MACE events occurred in 10.5% of patients in the control group compared with 7.3% in the intervention group, corresponding to a 46% reduction in the odds ratio with intervention (OR, 0.54; p=0.001).

The major therapeutic change in patients assigned to the intervention was the greater use of inhibitors of the renin-angiotensin-aldosterone system (p=0.02). There was a trend toward a lower level of low-density lipoprotein cholesterol in patients assigned to intervention (p=0.06), despite similar use of statin therapy, implying that compliance and adherence may have been improved with the intervention. The increase in BNP level over time was attenuated in the patients randomized to the intervention.

These results suggest that BNP may be a useful adjunctive tool to identify patients at risk for clinical HF or LVD but additional data is needed before this strategy is applied in routine clinical practice.