

NT-proBNP May Have Predictive Value in CAD

BY BRUCE JANCIN

SNOWMASS, COLO. — N-terminal pro-brain natriuretic peptide has a largely untapped potential for routine use in the office-based assessment of long-term risk in patients with chronic stable coronary artery disease.

Most physicians are familiar with NT-proBNP mainly as an in-hospital test for risk stratification and targeting therapy in the setting of acute coronary syndrome, but several years ago Danish investigators showed in a large longitudinal study that the cardiac biomarker is also an independent marker of mortality over the next dozen years in patients with stable CAD, Dr. Patrick T. O'Gara noted at a conference sponsored by the American College of Cardiology.

Indeed, NT-proBNP provided prognostic information above and beyond that imparted by the standard cardiovascular risk factors. For example, patients with a baseline NT-proBNP in excess of 455 pg/mL, placing them in the highest quartile, had an adjusted 2.4-fold greater risk of all-cause mortality during a median 9 years follow-up than those in the lowest quartile (a value less than 64 pg/mL).

A fourth-quartile NT-proBNP obtained in the physician's office was a stronger prognostic marker of all-cause mortality than diabetes, which conferred a 1.7-fold increased risk; cigarette smoking, with a 1.6-fold increase; or suspected heart failure, with a 1.8-fold elevated risk. Thus, the Danish findings broaden NT-proBNP's spectrum of clinical usefulness as a prognostic marker from the acute settings of the emergency department and coronary care unit to a population of intermediate-risk outpatients with stable chronic CAD, observed Dr. O'Gara of Brigham and Women's Hospital, Boston.

The study, conducted at the University of Copenhagen, involved 1,034 patients referred for coronary angiography because of signs or symptoms of CAD. During a maximum of 12 years and median of 9 years of follow-up, 288 patients died.

The mechanism underlying the association between NT-proBNP and long-term mortality risk in patients with stable CAD remains unclear. The association was independent of left ventricular ejection fraction and LV end-diastolic pressure, although it is possible that high levels of the biomarker reflect subtle LV remodeling detectable only by MRI or other high-definition imaging methods not employed in this study.

Another hypothesis advanced by the Danish investigators is that myocardial ischemia directly promotes NT-proBNP release (N. Engl. J. Med. 2005;352:666-75).

The Danish study was supported by the Danish Pharmacists Foundation. Dr. O'Gara indicated that he has no relevant financial interests. ■

Ablation for A Fib Trial Recruiting

BY BRUCE JANCIN

SNOWMASS, COLO. — The large multicenter CABANA trial, which is now recruiting, may be the last and best chance to learn if maintaining sinus rhythm confers a survival advantage over rate control in patients with atrial fibrillation.

CABANA (Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atri-

al Fibrillation) is randomizing roughly 3,000 patients with all types of symptomatic atrial fibrillation—paroxysmal, persistent, and long-standing persistent—to left atrial catheter ablation, antiarrhythmic drug therapy, or rate control medication. The primary end point will be total mortality with at least 2 years of follow-up.

Patients with atrial fibrillation (AF) should be encouraged to enroll in this

trial; it's a chance to receive catheter ablation as first-line therapy, should they be randomized to that study arm.

In contrast, current clinical practice is generally to reserve ablation therapy for patients who have failed at least one antiarrhythmic drug, Dr. Roger A. Winkle noted at a conference sponsored by the American College of Cardiology.

Catheter ablation as definitive treatment for AF has evolved over a rela-

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Indication

TWYNSTA is indicated for the treatment of hypertension, alone or with other antihypertensive agents. It may also be used as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. Base the choice of TWYNSTA tablets as initial therapy for hypertension on an assessment of potential benefits and risks including whether the patient is likely to tolerate the starting dose of TWYNSTA tablets. Consider the patient's baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared with monotherapy when deciding whether to use TWYNSTA tablets as initial therapy.

Hypotension

Volume depletion and/or salt depletion should be corrected in patients before initiation of therapy or start treatment under close medical supervision with a reduced dose, otherwise symptomatic hypotension may occur. Observe patients with severe aortic stenosis closely for acute hypotension when administering amlodipine.

Hepatic Impairment

In patients with impaired hepatic function, initiate telmisartan at low doses and titrate slowly, or initiate amlodipine at 2.5 mg. The lowest dose of TWYNSTA is 40/5 mg; therefore, initial therapy with TWYNSTA is not recommended in hepatically impaired patients.

Renal Impairment

Monitor carefully in patients with impaired renal function, especially in patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system (RAAS) (eg, patients with severe congestive heart failure or renal dysfunction); treatment of these patients with ACE inhibitors and ARBs has been associated with oliguria and/or progressive azotemia and, rarely, with acute renal failure and/or death. In patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen may occur.

Dual RAAS Blockade

When adding an ACE inhibitor to an ARB, monitor renal function closely. Use of telmisartan with ramipril is not recommended.

Other

Uncommonly, increased frequency, duration, and/or severity of angina or acute myocardial infarction have developed in patients treated with calcium channel blockers, particularly patients with severe obstructive coronary artery disease. Closely monitor patients with heart failure.

Adverse Events

In clinical trials, the most commonly reported adverse events with TWYNSTA that were more frequent than with placebo were peripheral edema (4.8% vs 0%), dizziness (3.0% vs 2.2%), clinically meaningful orthostatic hypotension (6.3% vs 4.3%), and back pain (2.2% vs 0%).

Special Populations

In clinical studies, the magnitude of blood pressure lowering with TWYNSTA in black patients approached that observed in non-black patients, but the number of black patients was limited. TWYNSTA is not recommended as initial therapy in patients who are 75 years or older, or who are hepatically impaired. In nursing mothers, nursing or TWYNSTA should be discontinued.

References: 1. Twynsta Pl. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2009. 2. Data on file, Study 1235.1, Boehringer Ingelheim Pharmaceuticals, Inc. 3. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289:2560-2572.

Please see Brief Summary of Prescribing Information on following pages.

tively short time from an experimental procedure to an important therapeutic option that provides cure or significant palliation in the majority of patients, with acceptable complication rates at high-volume centers with experienced providers.

The results are “vastly superior” to antiarrhythmic drug therapy in terms of maintenance of sinus rhythm, improvement in quality of life, and reduction of symptoms. That’s why CABANA employs ablation as state-of-the-art rhythm control therapy in a showdown against rate control and antiarrhythmic

drugs, explained Dr. Winkle, who is director of electrophysiology at Sequoia



The results are ‘vastly superior’ to antiarrhythmic drug therapy in terms of sinus rhythm and quality of life.

DR. WINKLE

Hospital in Redwood City, Calif. Theoretically, maintaining sinus

rhythm should reduce stroke risk, avoid the side effects of long-term anticoagulation, and improve survival.

However, “all of the studies of rate versus rhythm control with the medications we currently have available have been neutral. It’s possible that we can’t show a beneficial effect of sinus rhythm because we really don’t have agents that keep most people in sinus rhythm. Or alternatively, the current antiarrhythmic drugs and warfarin therapy that we use may cause enough harm to offset the benefits of being in sinus rhythm. We just don’t have the an-

swer to that,” the cardiologist said.

Secondary end points in the CABANA trial include AF recurrence, stroke, quality of life, and cost effectiveness. The principal investigator is Dr. Douglas L. Packer of the Mayo Clinic, Rochester, Minn. Participating sites are distributed geographically across the United States (www.cabanatrial.org). ■

Disclosures: The trial is funded by St. Jude Medical, Biosense Webster, and the National Heart, Lung, and Blood Institute. Dr. Winkle reported having no relevant financial interests.



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*According to the JNC 7, Stage-1 hypertension is defined as 140-159 mmHg SBP or 90-99 mmHg DBP. Stage-2 hypertension is ≥ 160 mmHg SBP or ≥ 100 mmHg DBP.³

†Standard deviation was 11.9/7.6 mmHg, TWYNSTA 40/5 mg; 13.2/7.9 mmHg, TWYNSTA 40/10 mg; 12.7/8.5 mmHg, TWYNSTA 80/5 mg; 14.2/7.9 mmHg, TWYNSTA 80/10 mg; 16.7/9.4 mmHg, placebo.²

ARB: Angiotensin receptor blocker. CCB: Calcium channel blocker. DBP: Diastolic blood pressure. SBP: Systolic blood pressure. JNC 7: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

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