Are Plasma Levels of Atrial Natriuretic Peptide, N-Terminal ProANP, and Brain Natriuretic Peptide Affected by the Presence of Coronary Artery Disease?

To the Editor:

We read with great interest the recent article by Bibbins-Domingo et al. on plasma brain natriuretic peptide (BNP) in outpatients with stable coronary disease. They concluded that elevated levels of BNP are independently associated with inducible ischemia in outpatients with stable coronary disease, particularly among those who have a history of myocardial infarction.

Previous studies have demonstrated that transient myocardial ischemia stimulates the secretion of atrial natriuretic peptide (ANP) and N-terminal ProANP (N-ANP); because of its longer half-life, N-ANP may be a better marker than ANP for the detection of high-grade coronary artery stenosis. However, whether plasma BNP levels are increased in patients with coronary artery stenosis who have normal left ventricular function remains unknown. To examine whether coronary artery stenosis affects plasma ANP, N-ANP, and BNP levels, we recently measured these peptide levels in 104 patients with normal left ventricular systolic function who had a suspected diagnosis of angina pectoris.

Plasma levels of all 3 of these natriuretic peptides were higher in patients with coronary artery stenosis (major coronary artery stenosis >75% (n=65) than in those without stenosis (n=39), whereas hemodynamic variables were similar. Multiple logistic regression analysis revealed that N-ANP (per 100 fmol/mL increase; odds ratio =1.9 [95% CI=1.2 to 2.6], P<0.01), but not ANP (per 10 pg/mL increase; odds ratio=0.9 [95% CI=0.5 to 1.2], P=0.41) or BNP (per 10 pg/mL increase; odds ratio=1.1 [95% CI=0.8 to 1.4], P=0.73), was independently associated with coronary artery stenosis after adjusting for clinical and demographic variables. Furthermore, we measured these natriuretic peptides before and 3 to 6 months after percutaneous coronary intervention in patients with myocardial infarction of recent onset (n=58). Plasma levels of ANP, N-ANP, and BNP significantly decreased in patients without restenosis (n=46) (ANP, 91±15 to 39±7 pg/mL; BNP, 134±28.9 to 41±9 pg/mL; N-ANP, 688±81 to 407±52 fmol/mL; all P<0.05).

In contrast, these natriuretic peptide levels did not change after coronary intervention in patients with restenosis (n=12) (ANP, 57±19 to 50±20; BNP, 102±35 to 57±13; N-ANP, 567±178 to 508±126; all NS). Our results support the findings of Bibbins-Domingo et al; however, we propose that N-ANP may be more useful for the discrimination of clinically significant coronary artery stenosis than BNP because of its different sites of production, mechanisms of release, and metabolic characteristics.

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Response

We thank Dr Nishikimi and colleagues for describing the results of their study demonstrating an association between N-terminal pro-atrial natriuretic peptide (N-ANP)—but not atrial natriuretic peptide (ANP) or brain natriuretic peptide (BNP)—and coronary artery stenosis. The authors conclude that N-ANP may be more useful than BNP for discriminating clinically significant coronary artery stenosis. We are pleased that their independent study supports an association between natriuretic peptides and coronary disease. However, we note that the authors’ study examined a different outcome (coronary stenosis) than our study (inducible ischemia). Because anatomic findings often do not correlate with severity of ischemia or risk of acute coronary syndromes,1 the association of N-ANP with coronary stenosis does not necessarily imply that N-ANP is more useful for discriminating clinically significant coronary disease than BNP. Moreover, the authors found similar declines in ANP, N-ANP, and BNP in patients after post-MI percutaneous interventions, suggesting that all 3 peptides are associated with ischemia. Regardless of potential differences between ANP, N-ANP, and BNP, results from both of these studies suggest a potential mechanism for the increased risk of future cardiac events associated with elevations in natriuretic peptides2,3 and may explain why tests for natriuretic peptides are not specific for ventricular dysfunction among patients with coronary disease.4,5

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Circulation. 2004;109:e331
doi: 10.1161/01.CIR.0000132588.63901.C1
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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