

Brain Natriuretic Peptide and Breathing Not Properly: The Merger of 2 BNPs

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Featured Article: Maisel A, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, Duc P, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;347:161–7.²

The idea for the Breathing Not Properly Study came from a preliminary study that we performed in our emergency department. I begged for devices to measure brain natriuretic peptide (BNP) from Biosite, an up-and-coming point-of-care company located in San Diego. The company's BNP marketing director, Scott Mader, made sure I had enough kits for our preliminary study (1). Our results showed 90% diagnostic accuracy! We found that many patients who were being followed for chronic obstructive pulmonary disease actually had heart failure (an echocardiogram doesn't always pick it up). Because this observation could be a game changer, we needed to convince Biosite to fund a multicenter trial, which had never before been done at a "diagnostic lab" company. If I have no other enviable traits, I do have perseverance, and I was finally able to tap loose the funds necessary for the study. With the help of Peter McCullough, we put together a simple but statistically robust protocol. We then traveled the US and Europe looking for just the right sites. I am also the ultimate of friendly arm-twisters. There was a promise of first authorships to all (this was kept), as well as being part of an important study.

The name of the trial, "Breathing Not Properly," actually came from one of my emergency department nurses at the Veterans Administration. In the midst of a dyspneic patient—recruiting frenzy one day, she remarked, "Oh God, here comes another breathing not properly patient." It stuck in my head, and although some at Biosite thought the name would belittle the study, I was sure it would not. I was right, and the acronym now has a robust place in the biomarker vernacular.

Executing the study entailed calls, personal visits, and lots of reassurance. After all, Scott Mader and 2 other individuals from Biosite were basically the contract reviewer officers. I remember right at the beginning of the study, I received a phone call at 0300. The doctor was asking if he could enroll a dyspneic patient. Blinking away my sleep, I said in a bothered voice, "Why wouldn't you? He is dyspneic isn't he?" "Uh, well, yes," came the response. "Then what?" I said, glancing at my beckoning pillow. "Well, he has a hatchet embedded in his chest!" Rest assured this patient was not, in fact, enrolled in the trial.

There was initial disagreement over who would analyze the data. I insisted that Paul Clopton, the statistician at the Veterans Administration and now the statistics editor for the *Journal of the American College of Cardiology*, and I do all analyses. It is fortunate that I won that battle. Shortly after submission to *The New England Journal of Medicine*, I received a phone call from the editor. He said he loved the study and was planning on a lead position with both an editorial and a perspective piece, but only if I could answer his one question the way he wanted. I held my breath. "Where was the data analyzed?" I exhaled through a toothy smile. "Right here at the San Diego VA." That was it. Done deal.

Many individuals feel that this publication heralded acceptance of natriuretic peptide concentrations. But I fully realize that a game-changing study is built on the backs of many others, scientists like John Burnett and Mark Richards, without whose groundbreaking work I never would have even been "in the game."

A few weeks ago I was lecturing the medical students, and one of them turned to his friend in the front row and said, "Hey, that guy is Mr. BNP." I smiled and then laughed when I replied, "That's 'Doctor BNP' to you!"

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² This article has been cited 1320 times since publication.

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Reference

1. Dao Q, Krishnaswamy P, Kazanegra R, Harrison A, Amirnovin R, Lenert LA, et al. Utility of B-natriuretic peptide (BNP) in the diagnosis of congestive heart failure in an urgent-care setting. *J Am Coll Cardiol* 2001;37:379–85.