

## Do we need brain natriuretic peptide determinations in emergency care?

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In response to increased ventricular volume or pressure, heart muscle cells increase the synthesis of pro-B-type natriuretic peptide (ProBNP) which, when secreted into the bloodstream, divides into two fragments. One is BNP itself, which has diuretic, natriuretic, vasodilatory and muscle relaxation effects. The other is the N-terminal proBNP (NT-proBNP), which is biologically inactive. The levels of both fragments can be determined analytically and, for practical purposes, used as markers of congestive heart failure (HF)<sup>1</sup>. This editorial will use the term BNP to refer to both forms.

BNP determination was introduced into clinical practice in 1994<sup>2</sup>. It is probably one of the most widely studied biochemical tests, generating numerous publications. This is because of its fundamental value for the diagnosis of HF, which remains a complex issue. The increasingly high prevalence of HF in Western countries constitutes a growing health burden that tests the effectiveness of emergency services<sup>3,4</sup>. Presumptive diagnosis of HF requires prolonged dedication of an experienced physician, with complete medical history, a thorough physical examination and analysis of signs based on specific training and a learning curve that is not always readily available. Finally, confirmation requires echocardiography which is also not always immediately available, despite being a non-invasive and relatively inexpensive diagnostic tool. Thus, the possibility of having a laboratory test allowing rapid and reliable results, without the need to involve other professionals, has aroused great interest<sup>5</sup>.

Our expectations, unfortunately, have only partly been fulfilled. BNP has shown good sensitivity for the diagnosis of HF, lower specificity and acceptable rates of positive and negative likeliho-

od<sup>6</sup>. All this means that the BNP test, despite showing remarkable overall diagnostic accuracy, is unfortunately not definitive. There are numerous circumstances that modify BNP levels and hinder the interpretation of test results in patients with suspected HF. These levels are influenced by age<sup>7</sup>, sex<sup>8</sup>, renal failure, acute coronary syndromes and conditions that increase right ventricular pressure such as pulmonary thromboembolism<sup>9</sup> or chronic obstructive pulmonary disease. The increase is less than expected in situations of sudden onset HF, such as flash pulmonary edema, or acute mitral regurgitation. And BNP does not show significant increase in HF where the left ventricle is not subject to increased pressure, such as in mitral stenosis. Other circumstances such as mild and treated HF, obesity and certain drugs, diet and exercise, all modulate plasma levels and make them difficult to interpret<sup>10</sup>.

The problem is that BNP was once projected as a dichotomous test where levels above a certain cutoff value would indicate a diagnosis of HF and lower levels exclude it. This expectation has not been met. Before the advent of BNP, clinicians knew that the diagnosis of a syndrome as complex as HF could not be established on the basis of only one of several parameters we used, including history of orthopnea, jugular venous pressure, a third heart sound on auscultation or a compatible chest X-ray, however much we analyzed the sensitivity, specificity or likelihood ratios of each one of them<sup>11</sup>. And the process involved in reaching a diagnosis of such a complex entity is imperfect. A presumptive diagnosis is a probability and often there is no absolutely definitive diagnosis, even after multiple tests in series or in parallel. In this context, BNP is one more test that

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helps us to establish the diagnosis, possibly with a higher accuracy than other tests previously available if we analyze them individually. Probably the most important diagnostic contribution of the BNP test is its very high negative predictive value, with low BNP levels virtually ruling out HF<sup>4,10</sup>.

Although BNP has not turned out to be the gold standard of HF diagnosis, it has been investigated as a useful tool for other objectives: as a prognostic marker at the time of initial diagnosis or after appropriate treatment, as a screening test for asymptomatic ventricular dysfunction, and even as a guide to treatment regardless of clinical manifestations<sup>12</sup>. In each of these areas, the BNP test has proved to be of interest, but not as a sole definitive marker that would allow us to ignore other signs and symptoms of HF<sup>6</sup>, and certainly not one that would allow us to do without echocardiography.

This issue of EMERGENCIAS contains a study carried out in various national emergency departments (ED) which examines the question of whether the BNP test is of interest in attending patients with suspected acute heart failure, and specifically focuses on its prognostic value for early mortality and ED revisits<sup>13</sup>. The novelty of this study is that not all the patients were admitted to hospital, which has only been evaluated in an indirect manner before. The conclusions are that BNP is a predictive marker of early mortality from a statistical point of view, but it has limitations for individual decision making. Another striking aspect is that BNP does not seem to be able to predict ED revisits, which contrasts with the findings of other studies<sup>14</sup>. But this could be because the reason for ED revisits was not analyzed; in a health system where ED visits are amongst the highest in the world, it is possible that the reason is unrelated to HF and this is a major confounding factor.

An unresolved issue of great importance is whether the BNP test is cost-effective in an ED. Most studies seem to show that it is<sup>15-18</sup>, but it is difficult to apply to our EDs the findings of studies usually carried out in other health systems. In addition, analytical studies tend to become less expensive as time passes (the cost of the BNP test is currently significantly lower than it was, say, five years ago). And the availability of the gold standard test in the ED has improved. Today, it is not uncommon to find EDs offering bedside echocardiography, performed by ED physicians themselves, possibly not of the same quality as those offered by conventional means, but still of interest.

Like most diagnostic tests, BNP must be used

appropriately and the results require interpretation, but it does provide important information. The cost is still high but not as high as it was some years ago. In this changing scenario where HF remains a challenge, it would seem that the argument for EDs not having the BNP test is less and less convincing. Without it, most experienced physicians can continue to diagnose HF with a high degree of certainty, but there are often circumstances which complicate the process, such as when the patient's medical history is missing or incomplete, or when the physical examination is hampered by lack of patient cooperation, or when basic complementary tests (chest X-ray, ECG etc.) are difficult to interpret for technical reasons. The answer to the question in the title could be: we can continue to do without the BNP test in the ED, but it would be highly desirable to have it.

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