To BNP or not to BNP

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This editorial refers to ‘Neurohormonal and clinical sex differences in heart failure’†, by S. Meyer et al., on page 2538

The burden of heart failure

Heart failure remains a major medical and social challenge despite the extraordinary progress in its diagnosis and treatment during the last 20 years. As a matter of fact, social factors such as the ageing of the population and the increase in longevity, both attributable to new treatments, will contribute to increase the burden of heart failure in future years. More than ever, we are in need of new, improved, and reliable methods for diagnosis and treatment guidance, which should be easy to use and are economically affordable.

Sven Meyer and colleagues, a highly experienced group in heart failure, have now explored the COACH registry data set (Coordinating study evaluating Outcomes of Advising and Counselling in Heart Failure), trying to gain a better understanding of neurohormonal and clinical sex differences in heart failure. Differences in the clinical characteristics and outcomes of heart failure in men and women have been a matter of controversy for years. The authors’ finding is that women in the registry presented better outcomes, but this was strongly influenced by the different biomarker profile between men and women. They studied a cohort of 567 patients with a comprehensive sample of biomarkers, but included the entire spectrum of heart failure from ventricular dysfunction to severe symptomatic patients and different modalities of heart failure upon hospital admission. Hence, the observations are very informative, but do not permit the refinement of the value of biomarkers in specific heart failure conditions. More interestingly, NT-terminal pro brain natriuretic peptide (NT-proBNP; a biomarker for cardiomyocyte stretching), and tumour necrosis factor-α receptor 1a (TNFαR1a) and growth differentiation factor 5 (GDF5; both biomarkers of inflammation) seem to be some of the most discriminative biomarkers for prognosis, with differences between men and women.

Biomarker levels help to understand the potential pathophysiological mechanisms of heart failure in a particular clinical setting, e.g. heart failure with reduced left ventricular ejection fraction (HFrEF) or preserved left ventricular function (HFpEF). A myriad of different biomarkers have been related to heart failure, exploring the role of inflammation, oxidative stress, remodelling, cardiomyocyte stretching, and renal function, among many others; not to mention the information rapidly arriving from systemic genotyping of patients with disease. In fact, we currently have far too many (Figure 1). Not to better understand the physiopathology and find new potential strategies for treatment, but simply too many to take into account in clinical practice. We need to select those with a clear added value for diagnosis, prognostic stratification, and treatment tailoring over the standard myriad of data that we routinely obtain from the clinical history of the patient and the accepted diagnostic tests such as biochemistry, ventricular function, or new imaging techniques. The new methodology should provide extra value, but without increasing the complexity and expense. The best biomarker would not characterize the disease because of a perfect relationship with the physiopathology of heart failure; but would be the one providing more accumulated useful information in clinical practice (Figure 1). It would be the one included in more registries, clinical trials, and more exposed to the scrutiny of its value in clinical practice; the one that better fills the gap between the bench and the bedside. That is what applies to NT-proBNP, so far.

The role of BNP in diagnosis of heart failure is nevertheless limited. Natriuretic peptides are secreted in response to a non-specific pressure load of any cardiac chamber; which is the case of heart failure, but also in systemic hypertension, pulmonary diseases, pulmonary embolism, atrial fibrillation, valvular disease, and even in some non-cardiovascular conditions such as renal failure. Therefore, its specificity for diagnosis is low. However, a normal level of BNP virtually excludes the diagnosis of heart failure. The challenge resides in the cut-off level, always a decision balancing sensitivity against accuracy and without full consensus yet. The general recommendation is to use BNP to help heart failure diagnosis when echocardiography or other imaging techniques are not reasonably available for the diagnosis of heart failure. Even in the presence of left ventricular dysfunction in patients with heart disease and clear ventricular function abnormalities, a BNP level within the normal limits virtually excludes heart failure as the cause of other suggestive complaints, mainly dyspnoea. It meaningfully becomes an invaluable asset in clinical practice for selected patients.

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The role for prognosis is even more clear. The release of BNP is part of a complex neurohormonal activation cascade trying to compensate for a functional or anatomical abnormality. Although BNP exerts vasodilatory and diuretic properties, an increase in BNP levels has been consistently associated with worse outcomes in heart failure patients, independently of the value of other prognostic biomarkers. It is of note that the need for refinement on this matter lies in the different modalities of heart failure, mainly HFrEF vs. HFpEF.

Perhaps the ultimate challenge for an ideal biomarker is to provide value for guiding therapy and this somehow should contribute to improving the quality of life and longevity of the individual patient. Some observations seem to support this hypothesis, but unfortunately others failed to demonstrate this value. Further high quality clinical research is needed in this field, and ongoing studies will certainly help to provide the right answer.

According to this information, the recent guidelines for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology recommend considering the measurement of natriuretic peptide [BNP, NT-proBNP, or mid-regional pro-atrial natriuretic peptide (MR-proANP)] to exclude alternative causes of dyspnoea in patients with suspected heart failure and to evaluate the prognosis. Curiously, this indication was labelled as a grade IIa recommendation with a level of evidence C in the guidelines, probably a weak recommendation for some readers but clearly reflecting a call for more research to better understand its final role in clinical practice.

All in all, biomarkers will play an important role in clinical practice and, so far, NT-proBNP provides the best information value in clinical practice.

Conflict of interest: none declared.

References


CARDIOVASCULAR FLASHLIGHT

One for the road...

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A 38-year-old male bartender without cardiovascular history, who had been consuming alcohol for several hours previously, was referred with suspected myocardial infarction by the mobile acute chest pain unit to the emergency department. Sudden onset acute thoracic pain occurred after he had won a game contest, held between clients, by being the first to finish a full glass of beer, just before the bar closed. Upon arrival, the clinically intoxicated patient complained of severe chest discomfort, hiccups, vomiting, and dysphagia. Normal haemodynamic parameters were noted. Electrocardiography revealed sinus tachycardia and normal pattern of repolarization. Chest X-ray, however, indicated the presence of a serrated cap of a beer bottle that the patient had accidentally and unconsciously swallowed and was now stuck at the upper level of the oesophagus. (Panel A and B) After being sedated the patient was intubated to secure the airway, and upper oesophageal endoscopy was performed subsequently. By using an endoscopic polypectomy snare, the cap was retracted into the larynx from where it was extracted under the direct laryngoscopic view with a Magille clamp. Apart from a mild headache, further clinical course was uneventful. This case supports current recommendations advocating a daily maximum of two units of alcohol for men and one for females, as additional quantities may cause harm in more than one way.

 Panels A and B. Chest radiograph. The postero-anterior view (A) and lateral view (B) indicate the presence of a serrated cap of a beer bottle (arrow) in the upper oesophagus, posterior to the trachea.

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