In reply: The emerging value of molecular forms of B-type natriuretic peptide in heart failure

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We would like to commend Drs Yang and Wang for their forward-thinking perspectives and positive implications of the clinical measurements of molecular forms of B-type natriuretic peptide (BNP) (1). We share the view that these processed forms of BNP can provide beneficial clinical information for cardiovascular disease prognoses and therapeutic monitoring with an emphasis on personalized medicine. We have previously demonstrated the prognostic capabilities of BNP molecular forms in the acute setting through measurement in acute heart failure (HF) patients (2), and support the further investigation of these forms across cardiovascular conditions.

Through advanced immunocapture methods and analytical technologies, we now know that there are in fact a range of BNP molecular forms (3) and that clinically applied immunosorbent assays are reflective of multiple forms and not solely the bioactive parent BNP 32-amino acid peptide [1-32] (4). From a mechanistic standpoint, this suggests that only a proportion of clinically measured BNP might be contributing to functional effects. This view is supported by the demonstration that BNP 3-32, as one of the major circulating molecular forms, exhibits reduced bioactivity when compared to BNP 1-32 (5). It is not currently known whether a common distribution of BNP molecular forms is found amongst patients, however through our analyses we are aware that BNP 5-32 is more readily detected and shows improved prognostic abilities when compared to BNP 4-32 and 3-32 in acute HF (2). In addition, BNP 5-32 has been previously shown to show greatest association with clinical BNP measurements (r=0.81) (4), further suggesting its role as a major circulating form.

The premise for the future role of BNP molecular forms in a clinical setting is highlighted in our cohort of acute HF patients and advocates the development of a commercial assay that can measure a panel of molecular forms. The identification and measurement of BNP forms is currently centred on the use of MALDI-ToF mass spectrometry (6) which provides high levels of sensitivity but with the caveat of low sample throughput. The development of an assay to reproducibly measure BNP forms while increasing the throughput of sample processing would be a further push towards a clinical setting.

The future measurement of BNP molecular forms is expected to provide added benefits in cardiovascular disease prognoses but also allow for an improved understanding of the profiles of individual forms, their kinetics and dynamics, and their responses to treatment. For example, the formation of BNP 4-32 is attributed to the effects of corin and it has recently been identified that changes in corin expression are present in myocardial infarction patients that link to infarct size, presence of STEMI and subsequent poor outcomes (7).

We believe that in the era of personalized medicine, the clinical measurement of BNP molecular forms would offer additional information in cardiovascular disease conditions, allow for risk stratification and aid the understanding of the underlying mechanisms of BNP peptide processing in response to treatment and disease management strategies.

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