Diastolic dysfunction and ANP/BNP levels

See page 1694 for the article to which this Editorial refers

Doctors who work in diabetes or in hypertension have the luxury of one parameter (blood sugar or blood pressure) against which the diagnosis can be made and the treatment monitored. Sadly, in cardiology and especially in heart failure, we have no such single parameter to guide us.

Even if we restrict ourselves to systolic heart failure, there is not one single parameter. Traditionally, most large studies have used the left ventricular ejection fraction as their principal entry criteria, despite recognised limitations, such as a low left ventricular ejection fraction not even predict the development of heart failure in the SAVE study and it is not as good a prognostic predictor as left ventricular ejection fraction did not even predict the severity. For example, Hall et al. showed clearly that N-terminal pro atrial natriuretic factor values were predictive of a poor outcome over and above other predictors such as left ventricular ejection fraction. We recently found the same for BNP.

In this issue Yu et al. bring these two ideas together. In this paper, they studied 68 patients who had definite systolic heart failure. It is firstly important to realise that this paper is about diastolic function in patients with known systolic dysfunction. It tells us nothing about the entity of diastolic dysfunction in the presence of normal systolic function. In this paper they found that all but 7% of their patients with systolic dysfunction had diastolic abnormalities of some kind. The restrictive filling pattern described above was found in 62% of these patients. When they compared those with versus those without the restrictive pattern, plasma levels of ANP and BNP were much higher in those with the restrictive pattern.

References

More arrhythmias and death

More electrical inhomogeneity

More LV fibrosis (= less myocytes)

More wall stress

More ANP/BNP

More diastolic dysfunction

Figure 1  Hypothesis.

Unfortunately the two groups were not ideally matched for systolic function in that the left ventricular ejection fraction was significantly lower and the NYHA class significantly higher in the restrictive group. However, it must be said that the ANP/BNP differences were large while the left ventricular ejection fraction differences were small and that left ventricular ejection fraction probably becomes an even more unreliable measure of systolic function in the presence of a very stiff left ventricle. To explore this further, multiple regression analysis was undertaken but this gives the impression that ANP/BNP levels were more determined by traditional measures of systolic dysfunction than by diastolic abnormalities. A stepwise multiple regression analysis might have helped pick out whether the restrictive pattern per se increased ANP/BNP levels, irrespective of systolic function but I do not think Table 3 represents such a stepwise analysis. In any event, this study was probably under-powered to demonstrate such an effect.

Despite the above caveats, this paper does show that a restrictive pattern is associated with clinically more severe heart failure and with higher ANP/BNP levels. Clearly it does not sort out which is the chicken and which is the egg. Does a more restrictive pattern cause more heart failure or vice versa? It could, however, explain why two patients with the same left ventricular ejection fraction can have different natriuretic peptide levels. It opens the door towards the possibility that at any given left ventricular ejection fraction, the increased prognostic information which can be obtained from ANP/BNP occurs because higher ANP/BNP levels reflects a more restrictive LV filling pattern, which itself alters prognosis. Alternately, this added prognostic information might be obtained more easily from measuring the E deceleration time at the time of echo assessment rather than measuring ANP or BNP.

Clearly it will require more and larger studies to pick out individual prognostic influences in a disease such as chronic heart failure where abnormalities tend to run in parallel so that nearly everything you measure becomes more abnormal, the more severe the disease. One hypothesis which might help explain these apparent relationships is illustrated here (Fig. 1). The ultimate culprit might be fibrosis replacing myocytes. Such left ventricular fibrosis might lead in parallel to worse systolic function and to a more restrictive pattern of left ventricular filling. Both of these will increase wall stress which is the ultimate cause of increased ANP/BNP levels. At the same time more patchy left ventricular fibrosis might cause more electrical inhomogeneity, more arrhythmias and more cardiac deaths. If this hypothesis is anywhere near the truth, we should look at it to see which parameters in it are feasible to measure in clinical practice. Myocardial fibrosis or wall stress may be the most desirable things to measure conceptually but in terms of ease of measurement, we are left with either ANP/BNP or echo parameters of systolic and diastolic function as the most feasible.

The work of Yu et al. and Pinamonti et al. nudges us gently towards including measures of diastolic function in our prognostic model for patients with known systolic heart failure but a lot more work would be required for this concept to gain universal acceptance.

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References


