N-terminal proBNP — the most cost effective way to identify post myocardial infarction left ventricular dysfunction?

See page 1514 for the article to which this Editorial refers

The idea that plasma levels of natriuretic peptides might be clinically useful to identify cardiac patients at high risk has been around for a long time and has attracted much attention. It is an idea which has always appealed more to non-cardiologists, especially family practitioners than to cardiologists. Understandably, cardiologists have more access to echocardiography than other doctors and prefer the more detailed information on cardiac structure and function which come from echocardiography. Non-cardiologists are more often in the business of trying to decide which patients to refer to cardiologists and it is here that plasma levels of natriuretic peptides are likely to be of benefit. Hence non-cardiologists are often more attracted to the idea of natriuretic peptide screening than are cardiologists.

The above is one of the reasons for the slow uptake of natriuretic peptide levels into clinical practice. Another reason is that natriuretic peptide experts appear to keep changing their minds on which natriuretic peptide level provides the best clinical information. Initially, it was ANP, followed by N-terminal proANP followed by BNP. Now there is N-terminal BNP. The paper in this issue on N-terminal BNP by Talwar et al.[1] adds greatly to the information required to decide which peptide to sample, when to sample it and how to interpret its value and I will discuss these issues below. However, perhaps the most important contribution to this whole debate comes from one sentence in their discussion where they say, ‘assays of N-BNP are highly cost effective, each test costing under £1, compared to the cost of echocardiography (£60-£80).’ No doubt, experts will argue about these precise costs, but even if they are only ballpark figures, it is very striking that there is a 70 × cost difference between these two tests. Since we all now live and work in health care systems which are concerned about spiraling costs, such a cost difference cannot be ignored. It could even cause health service managers and health economists to become interested in natriuretic peptide screening of patients before echocardiography. They could justifiably argue for a greater use of natriuretic peptide screening in certain circumstances in order to reduce the spiraling demand for echocardiography. Perhaps this one sentence from Talwar et al.[1] will ignite a long overdue debate on this topic. It is often said that ‘money talks’ and perhaps nowhere is this more true than in the funding of health services in the 21st century.

Since cost was not the main thrust of the paper by Talwar et al.[1], it would be unfair on the authors to dwell unduly on this, especially since the paper does have some other important messages. The main point addressed by the authors is when, after a myocardial infarction, should the blood sample be taken. They show that there are two peaks in N-BNP (at 14–48 h and at 121–192 h) and that the best discriminator for left ventricular dysfunction is the trough sample in between these two peaks. As an aside, it is intriguing that no-one ever established in nearly so much detail what is the best time point after a myocardial infarction to do echocardiography in terms of its ability to predict long-term prognosis. There are some minor limitations to this work, which are discussed by the authors and are worth mentioning. It would have been helpful to do a head-to-head comparison of the new N-terminal BNP assay with the older assay of BNP itself. In the only previous paper where a head-to-head comparison was made, both N-terminal natriuretic peptide and BNP performed equally well[2]. The other point that is not clear from the paper is how exactly the 60 patients studied were selected. It does not appear to be wholly random. The point here is that the performance of any test in clinical medicine is critically dependent on the pre-test probability of there being an abnormal result. Even despite that, doctors have to know whether to apply a new test to all-comers or to a selected group of patients and if so, how to do the selection. No doubt, these are issues which will be resolved by further research.
One of the other problems which dogged natriuretic peptide research earlier was the rather unrealistic idea that one single cut-off value would be >95% sensitive and >95% specific at identifying left ventricular dysfunction. This was always unlikely especially since cut-off values for left ventricular ejection fraction are arbitrary and controversial, ranging from 30% to 45% in different studies. Against this backdrop, N-BNP performs well as it outperforms all else in a multiple regression analysis and the negative predictive value is 91%, albeit the positive predictive value is lower at 41%. Based on these results, one could suggest that N-BNP is used to pre-screen patients for echocardiography. Alternatively, if N-BNP identifies poor prognosis accurately (as is likely — see below) then one could suggest the use of ACE inhibitor therapy both in those with clinical failure and in those with a high N-BNP but no clinical failure. One could even devise an algorithm as below

No doubt, the above would appeal to health service managers keen to contain costs. It would be intriguing to apply the above algorithm to the data of Talwar et al. and others to see not only what the cost saving would be in terms of reduced echocardiography but also to see how many patients (if any) with left ventricular dysfunction would be missed and whether any factor(s) could be identified to select the few who still need echocardiography. This whole debate will, however, move on (as all debates do). The poor outcome end-point chosen in Talwar et al. was a little unusual i.e. death or wall motion index <1.2 at 6 weeks. This was partly because there only were four deaths in the cohort at the time of study. Nevertheless, future analysis should focus on the ability of N-BNP to predict poor outcome in terms of clinical end-points only, such as death and/or hospitalization. From previous data, one would suspect that N-BNP will perform even better as a prognostic indicator than as a diagnostic indicator.

However, there is another whole reason why this debate might move on and that is the HOPE study. When all the post myocardial infarction studies of ACE inhibitors came out in the early 1990s, two camps developed. One camp suggested that ACE inhibitors should be given to all post myocardial infarction patients whereas the other camp suggested that it was more cost effective to select post myocardial infarction patients for ACE inhibitor therapy on the basis of whether the patients had left ventricular dysfunction or not. Over the years, the latter camp probably won the argument. The HOPE study could change that. Although the HOPE study did not specifically recruit patients in the immediate post myocardial infarction phase, it still has the wider implication that perhaps all patients with ischaemic heart disease should receive an ACE inhibitor, irrespective of their left ventricular dysfunction. If so, a myocardial infarction might well be the first manifestation of ischaemic heart disease in a proportion of patients. If one accepted this latter argument, then the need to screen post myocardial infarction patients with anything (including an echocardiogram) could
be seen as unnecessary. We are really only in the opening salvos of the debate which will inevitably rage as to how the HOPE study should influence clinical practice. It may well fall to the health economists to tell us which patients should receive the HOPE strategy of universal ACE inhibition despite normal left ventricular function. Since no conclusions can yet be drawn on how widespread the HOPE results should be applied, we should not yet (if ever) abandon the tried and tested custom of selecting post myocardial infarction patients for ACE inhibition on the basis of their left ventricular function and it is to this latter question that the data of Talwar et al.\[1\] make a major contribution.

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References


Joint efforts across national boundaries between professional organizations in cardiovascular medicine: one way into the future

See page 1502 for the article to which this Editorial refers

Medicine is international in the truest sense. With one of its origins in the Hippocratic oath, the practice of modern medicine has as its foundation the commitment of physicians to treat the sick to the best of their ability. Moreover, this commitment means that physicians in every country in the world are to care for the sick without consideration to the race, religion, socioeconomic class, or political persuasion of their patients.

Now, more than ever before, we are witnessing an openness and a spirit of cooperation in the medical world that has broken down closed international barriers. Visits by physicians from the United States to the former U.S.S.R. and from other western countries to the previously isolated Republic of China, served to engender mutual trust between medical professionals. Unlike the past, the art and science of medicine can now basically be disseminated without geographic restrictions. Since the recent and remarkable innovations in the field of electronic communication via the Internet, new and important medical knowledge is now globally available within amazingly short periods of time following discovery and scientific reporting. Thus, medicine has, in many ways, paved the way for global cooperation by its mere nature of serving the sick human being, whoever and wherever the sick individual resides.

Despite the progress made, there are many fields of medicine in which even greater cooperation and deepened relations can be achieved. The American College of Cardiology (ACC) and the European Society of Cardiology (ESC), two of the most distinguished professional organizations in cardiovascular medicine, realized this challenge and acted correspondingly. Several years ago, together with the American Heart Association (AHA), an initiative was taken to conduct Joint Leadership meetings of the three organizations biannually to discuss topics of interest that would benefit patients with cardiovascular disease. The initial emphasis was focused towards understanding each organization and its cultures, traditions, and objectives. Although there are many historic, cultural, and linguistic differences within Europe and between Europe and the United States, the three organizations share similar visions and goals from which to plan collaborative activities, with the ultimate goal being to improve patient care.

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