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Mechanism of a Hypertensive Response to Exercise

Mottram et al. (1) recently reported in the *Journal* new and unexpected findings: that a hypertensive response to exercise (systolic blood pressure >210 mm Hg in males and >190 mm Hg in females) in normotensive and hypertensive subjects is associated with subtle defects in systolic left ventricular (LV) function. A number of possible mechanisms were proposed.

Another explanation, not canvassed, relates to the effects of wave reflection on the pattern of systolic LV ejection, and on amplification of the aortic pressure wave to the site of pressure recording in the brachial artery.

Amplification of the pressure wave to the brachial or radial artery can be substantial during exercise, with one study showing peak difference of 80 mm Hg between aortic and radial peak pressure during maximal exercise (2). The degree of amplification depends on ejection period, being greatest when this is short, and least when it is long (3–5). Amplification of the pulse wave is attributable to wave reflection within the upper limb (3–6).

Most wave reflection returning to the heart comes from the lower part of the body (trunk and lower limbs) (6). This appears to be maintained during exercise in patients with systolic LV dysfunction (7). However, effects of wave reflection on the heart depend on the ability of the heart to eject against pressure. With impaired LV contractility, reflection has a greater effect on flow than pressure (8), and this restricts late ejection, causing shortened ejection, with accompanying decrease in stoke volume. The shortened ejection in severe heart failure is responsible for absence of systolic augmentation and appearance of the classic "dicrotic" pulse waveform (6,9).

It is quite possible that this mechanism is responsible for the findings of Mottram et al. (1), namely that increased wave reflection during the challenge of exertion causes greater reduction than usual in ejection duration, and that this leads to greater amplification of the pulse in the upper limb, and a greater recorded systolic pressure in the upper limb.

Finally, such a hypothesis could be tested by measuring ejection duration during exercise, and/or by estimating the aortic systolic pressure from the upper limb waveform. Have the investigators considered measuring ejection duration or central systolic pressure?

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Please note: Dr. O'Rourke is the Director of Atcor Medical, manufacturer of instruments for analysing the arterial pulse.

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REPLY

We thank Dr. O'Rourke for his comments in response to our study. Our report demonstrated that sensitive new myocardial measurements in normotensive patients who have a hypertensive response to exercise have abnormal left ventricular (LV) systolic and probably also diastolic behavior (1). We proposed that this phenomenon likely represents intrinsic damage to the myocardium, most probably from chronic exposure to "high-normal" levels of systemic blood pressure, which was present in these patients (1). Clearly, histological examination of myocardial tissue for hyperten-

sive changes such as interstitial fibrosis would advance our understanding of the relevant mechanisms.

Dr. O'Rourke makes the important point that systolic pressure measured at the brachial artery is significantly influenced by wave reflection, and that central aortic pressure is a more important influence on LV systolic function. Central aortic pressure is influenced by arterial stiffness (2), but our preliminary findings are that, while arterial compliance (measured using the pulse pressure method using radial artery tonometry) was less in patients with a hypertensive response to exercise compared with controls (3), it was not related to indices of LV systolic function. Moreover, work in progress suggests that augmentation index using carotid tonometry is no different in those with a hypertensive response to exercise and control subjects. Thus, although we agree with Dr. O'Rourke that measurement of LV ejection duration or estimation of aortic systolic pressure during exercise may provide insight into the mechanism of a hypertensive response to exercise as recorded with cuff blood pressure at the upper limb, our preliminary data do not support a major association of LV systolic dysfunction with central hemodynamics.

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Brain Natriuretic Peptide as a Predictor of Sudden Cardiac Death in Patients With Myocardial Infarction

We read with interest the study by Tapanainen et al. (1). The researchers introduced the brain natriuretic peptide (BNP) as a good predictor of sudden cardiac death (SCD) after acute myocardial infarction (AMI). In their study, BNP level of the patients with AMI was used to predict SCD. The incidence of SCD after the mean follow-up of 43 ± 13 months was 3.1%. The mean BNP level in patients with SCD was 54.4 ± 76.1 pmol/l and it was 26.1 ± 28.0 pmol/l in survivors. They found that a BNP level of 23.0 pmol/l was the best cut-off point to predict SCD. In another new study by Wang et al. (2), higher BNP was also associated with increased risk of overall death. The investigators reported a 27% increase in the risk of death with each increment of 1 SD in log of BNP level.

We know from the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) investigators that the survival of postmyocardial infarction patients with ejection fraction (EF) <30% will improve with prophylactic implantation of a defibrillator (3). It means that irrespective of BNP level, post-AMI patients with low EF will derive benefit from defibrillator implantation. Approximately one-third of the patients with prior infarction, left ventricular EF <40%, and spontaneous nonsustained ventricular tachycardia (VT) have inducible sustained VT, predicting 6% to 9% per year risk of sustained VT or SCD. A defibrillator reduces this risk to 3% to 5% per year (3,4). An EF between 30% to 40% is a gray area for defibrillator implantation, and this is the area that needs more clarification.

The studies have shown that BNP can probably be a good predictor of death, especially SCD, after MI. If we know the value of this predictive role in post-myocardial infarction patients with EF between 30% and 40%, we may be able to use it as a guide to defibrillator implantation decision. In the study by Tapanainen et al. (1) the mean EF of patients with SCD was 39.9 ± 10.8%. It seems that most of the patients in the study had an EF >30%, but separate analyses for different EF levels were not shown. We believe that if the researchers could perform a separate analysis for the patients with EF between 30% and 40%, the role of BNP level in predicting SCD in non-MADIT II patients might be more clearly established.

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