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point, ED is further defined as mild (22 to 25), mild-to-moderate (17 to 21), moderate (11 to 16), and severe (<10) (3). In the Kaiser et al. (1) study, "normal" subjects had a mean (±SD) score of the IIEF erectile function domain of 21.3 ± 5.3. Assuming a normal distribution, this means that almost 80% of normal subjects were below the cut-off for ED, of whom 40% likely had an IIEF score <20 (mild-to-moderate ED) and 10% <15 (moderate ED). Thus, many "normal" subjects were actually impotent, although to a lesser degree than the true ED group. However, penile color Doppler sonography (the only test that might have further differentiated the two groups) was not performed in normal subjects, and this makes any comment conjectural.

If this observation holds true, differences in the vascular response between groups should be reconsidered. In fact, if the dilation response of "normal" patients with ED is combined with dilation response of the real ED group, one would expect to obtain a higher mean value of percent vascular dilation. For example, percent dilation at 60 s after cuff release was 2.4 ± 0.5 versus 3.7 ± 0.5 in the ED and normal group, respectively. If combined, a mean value of 3% would reasonably become evident. This result, to still be significantly lower, would require normals to show an even higher dilation response, about 4% to 4.5%. This figure seems to be a rather unusual response after wrist occlusion (4).

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REPLY

Dr. Montorsi and colleagues express concerns over the International Index of Erectile Function (IIEF)-15 data presented in our study (1). We inadvertently stated that the data presented were the erectile dysfunction (ED) domain of the IIEF-15, but in fact the data cited in our report were an average of each individual domain of the IIEF-15. In response to their letter to the editor we went back to the raw data and calculated both the ED domain of the IIEF-15 and the IIEF-5 (an abbreviated version of the IIEF-15). These results are presented below.

The IIEF-15 domain consists of six questions (1, 2, 3, 4, 5, and 15) with a maximum score of 30 and a cut-off of <25 for ED (2). The ED group in our study had an IIEF-15 ED domain score of 16.1 versus 26.8 for the normal group ($p = 0.000001$).

The IIEF-5 is a validated brief version of the longer questionnaire (questions 2, 4, 5, 7, and 15 of the IIEF-15) (3,4). These five questions have been found to discriminate most highly between men with and without ED. The maximum score for the IIEF-5 is 25, with a cut-off of <21 for ED. The ED group in our study had an IIEF-5 of 12.9 versus 22.3 for the normal group ($p = 0.000001$).

We appreciate the opportunity to clarify this issue. Based on the results listed above for the ED domain of the IIEF-15 and the IIEF-5, our patients had significant symptoms of ED and our control subjects did not have ED. Therefore, the significance of our original observations is valid, and no further reassessments of the data are warranted.

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Exercise Release of Cardiac Natriuretic Peptides Is Markedly Enhanced When Patients With Coronary Artery Disease Are Treated Medically by Beta-Blockers

We read with interest the recent study by Marie et al. (1), which concluded that patients with chronic coronary artery disease exhibited much higher exercise release of (ANP) and brain natriuretic peptide (BNP) when they were treated with beta-blockers. Exercise-related increase in natriuretic peptides had been reported across a majority of patients undergoing exercise treadmill test for evaluation of ischemic heart disease (2–5). The investigators postulated that the mechanisms of enhanced natriuretic peptide release secondary to beta-blockade may be related to exercise-induced increase in wall tension and cavity size. However, the researchers did not report the presence of reversible ischemia among the patients who were receiving beta-blocker therapy.

We recently reported (6) that exercise-induced increase in B-type natriuretic peptide was more prominent in patients with evidence of reversible ischemia on single-photon emission computed tomography (SPECT). It is therefore possible that the presence of exercise-induced reversible ischemia may serve as a confounding factor in this patient population, and we wonder whether the BNP rise among patients receiving beta-blockers during exercise is significant if the data are adjusted for presence of reversible ischemia.

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REPLY

When we started our study, we hoped that an enhanced secretion of atrial natriuretic peptide (ANP) and/or brain natriuretic peptide (BNP) might allow for detecting exercise ischemia. However, as it was already pointed out in our report, myocardial ischemia was documented by exercise-single-photon emission computed tomography (SPECT) in 63 of our 104 patients with coronary artery disease, and this ischemia was not a predictor of the exercise increase in blood levels of either ANP or BNP (1). More precisely, in the 63 patients with SPECT-ischemia, the difference between exercise and rest concentrations of BNP was, on average, 14 ± 20 ng/l. Equivalent values were observed in patients with normal SPECT: 14 ± 35 ng/l. By contrast, much higher values were observed in the remaining patients showing SPECT-necrosis: 49 ± 55 ng/l ($p < 0.001$).

As it was already discussed in our study (1), this is mainly an acute release of peptides from secretory granules that is likely to allow a prompt exercise rise in the blood concentrations of peptides. Therefore, this rise depends on 1) the amount of peptides, which may be previously stored within secretory granules, and 2) the mechanism of peptides release from these granules.

Granule storage is known to rise in parallel to the resting blood concentrations of natriuretic peptides and to the level of left ventricular dysfunction. This is presumably the reason why we found that the rest concentration of peptides was a main predictor of the exercise increase in peptide concentration. For both ANP and BNP, however, rest concentra-