

Additionally, the SF-36 used by the researchers as an index of quality of life is, like the BDI, comprised of both mood and somatic items. The investigators report a significant correlation between the BDI and the SF-36; thus, they conclude that depression is associated with lower quality of life in HF patients. The overlapping domain items in the BDI and SF-36, however, may potentially confound this correlation, as the statistical association might, at least in part, reflect the degree to which *the scales themselves* correlate.

Depression and quality of life in patients with HF are significant public health issues that clearly warrant further investigation. As scientists, we must successfully grapple with the thorny issues of construct and scale validity within this population (e.g., "what is the nature of depression in HF?" "what is a validated measure of depression in HF?") if our research is to advance both the science and the standard of care for HF.

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doi:10.1016/j.jacc.2004.09.016

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## REPLY

We agree with the comments of Dr. Fauchier regarding our recent study (1) suggesting that many factors influence the prevalence of depression in patients with congestive heart failure (HF). However, it should not be assumed that a patient with a longer duration of symptoms is more likely to be depressed. It is just as likely that patients may become more adjusted to their situation, resulting in less depressive symptoms. Although it is difficult to determine duration of symptoms reliably, we did not attempt to do so; thus, we encourage others to test these hypotheses.

As indicated by our previous study referenced by Dr. Fauchier, we believe that defibrillators (ICDs) may have important psychological consequences (2). Because more ICDs are likely to be implanted owing to the SCD-HeFT study (3), it is crucial to

understand their psychological impact. For this reason, we obtained and are analyzing data from a substudy of SCD-HeFT addressing this issue.

We also agree with Dr. Ahmed that a collaborative model of treatment should be used in all patients with congestive HF. It is thus important that primary care physicians (including gerontologists) understand that patients who are still symptomatic despite treatment should be referred to a specialist in HF regardless of the patient's age.

One can debate Dr. Ahmed's assertion that depression is more common in the elderly; the data he references suggest that major depression is less common, whereas "minor" depressive symptoms may be more common (4,5). The current study involved many patients under age 65 years, dictating use of an instrument appropriate for a broad age range. However, we do not consider determination of the exact prevalence of depression in various groups as the important result of our study. Rather, our findings emphasize the difference in patterns of depression between patients with severe HF and the general population. Furthermore, we demonstrated (in the wide range of patients studied) that depression, as quantified by standard questionnaires, was extremely common in all groups. In our sample, 53% of those under age 65 years and 43% of those age 65 years and older reported symptoms of depression.

As Dr. Freudenberger and colleagues are well aware, the interaction of depression and symptoms of HF is complex; three of the co-authors of our manuscript (S.S.G., M.L.F., S.R.) co-authored a publication with two of them (R.F., C.S.), which demonstrated that patients with depression believe themselves to be more ill even when there are no objective criteria supporting this perception (6). Furthermore, as Dr. Ahmed's letter points out, diagnosis of depression is affected by many variables, including age, gender, and race. Indeed, any diagnosis of depression is, by definition, arbitrary. Thus, determination of the exact prevalence of depression can be debated ad nauseam, leading to obfuscation of the important points: depression is common and diagnosis may be impacted by various demographic factors. Although it is unreasonable to expect all patients with HF to be screened by psychiatrists, the Beck-Depression Inventory (BDI) is an excellent screening tool, and awareness of the prevalence of depression can lead to treatment and improved quality of life.

Dr. Freudenberger and colleagues are of course correct that physical components of the scales might be influenced by the physical limitations of HF. It is for this reason that we reported the various subscales of both the Minnesota Living With Heart Failure (MLWHF) and SF-36 questionnaires. Both the emotional and physical subscales of the MLWHF (a disease-specific quality-of-life questionnaire) exhibited extremely close correlations with the BDI. Similarly, various components of the SF-36, including those not influenced by physical limitations, strongly correlated with the BDI.

Depression may contribute to symptoms in any HF patient. Treatment efficacy will probably vary based upon age, gender, race or other factors, and these variables need to be assessed when intervention trials are performed. We now know, however, that consideration of the possible impact of depression upon symptoms is essential for all patients with HF.

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doi:10.1016/j.jacc.2004.09.017

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## Clinical Efficacy of Sildenafil in Primary Pulmonary Hypertension

In the report entitled “Clinical Efficacy of Sildenafil in Primary Pulmonary Hypertension: A Randomized, Placebo-Controlled, Double-Blind, Crossover Study” (1) the investigators cite an impressive short-term improvement in exercise capacity in patients with pulmonary arterial hypertension (PPH) and who are taking daily oral sildenafil. The researchers compare their patients’ improvement in exercise capacity with sildenafil to that of prior studies of oral bosentan, oral beraprost, and aerosolized iloprost. Although their earlier uncontrolled study, which used 6-min walk testing, suggested an improvement in walk distance of 40% over baseline (2), their more recent placebo-controlled study, which used submaximal exercise duration on a treadmill, showed a 44% increase in exercise time. This improvement was favorably compared to bosentan, beraprost, and iloprost, whose improvement in 6-min walk distance ranged from only 12% to 21%.

We applaud the investigators’ choice of measuring exercise endurance over a 6-min walk distance as a measure of exercise capacity end point for patients with PPH. However, we believe that these comparisons of sildenafil with other pulmonary vascular drugs should be interpreted cautiously, because: 1) the patient population in each study was not the same and 2) the 6-min walk distance and treadmill exercise endurance times are not comparable in terms of percent change. Oga et al. (3) have shown that submaximal exercise endurance time is a much more sensitive indicator of change in exercise capacity than the 6-min walk distance or peak  $\text{VO}_2$ . In that study, a 19% increase in exercise duration paralleled a much smaller, although significant, 1% increase in 6-min walk distance after treatment of chronic obstructive

pulmonary disease patients with an inhaled anticholinergic agent.

In measuring exercise capacity, the percent improvement in endurance time likely depends on the level of exercise, particularly with respect to the chosen exercise protocol (constant vs. incremental work rate protocol). Thus, in this latest sildenafil study, the 44% increase in exercise *duration* probably overestimates the improvement that would have been seen had the 6-min walk *distance* been used to measure exercise capacity.

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doi:10.1016/j.jacc.2004.09.010

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## REPLY

We appreciate the interest of Drs. Oudiz and Wasserman in our study (1). Our primary objective was to compare sildenafil with placebo in improving the exercise capacity in patients with primary pulmonary hypertension. From this study, we did not mean to conclude that sildenafil is superior to other pulmonary vasodilators like bosentan; beraprost, iloprost, and others.

Improvement in exercise capacity can be measured by different means including 6-min walk distance, submaximal exercise time, and maximum oxygen uptake during exercise ( $\text{VO}_2$  max). These tests measure different physiological parameters. In a group of patients treated by the same intervention, different tests may demonstrate different degrees of improvement depending upon the method chosen. Even different exercise protocols may give different results. As was pointed out, nearly 40% improvement in exercise time using the Naughton protocol need not result in similar degree of improvement in 6-min walk distance. Interestingly, however, apart from our initial study, other investigators also have reported a similar degree of improvement (ranging from 30% to 50%) in 6-min walk distance with sildenafil in pulmonary hypertension patients (2–5). It is possible that the exercise on treadmill test using the Naughton protocol may give similar results to the 6-min walk test, unlike the kind of exercise protocol used by Oga et al. (6) in their studies.

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