time of surgery largely explains the survival differences between nonsmokers and patients who quit smoking.

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Ideal Weight, Body Composition and Lipid Levels: An Unresolved Dilemma?
Osman et al. (1) have shown that in chronic heart failure (CHF), peak VO2 corrected for lean body mass is a more powerful predictor of clinical outcome than the traditional peak VO2 adjusted for total body weight. We thank the authors for addressing this important issue, since the estimation of exercise capacity is significantly influenced by body fat content (2). There are, however, several points we would like to comment upon. In addition to the findings of Osman et al. (1), we found that mildly obese CHF patients had a better prognosis (3). Although Osman et al. (1) demonstrated that subjects reaching the set end points had significantly reduced body fat mass, they did not provide statistical data regarding the impact of body fat mass on prognosis. Of note, the majority of subjects in their study had mild-to-moderate CHF and an average body weight of 89 kg (BMI [body mass index] 28.9 kg/m2), in keeping with metabolic stability. However, CHF is increasingly recognized as a metabolic syndrome with both fat and muscle mass being reduced during disease progression.

Osman et al. (1) state that fat tissue is metabolically inactive, and this is certainly true in the setting of acute exercise testing. Alternatively, fat mass may be an indicator of preserved metabolic efficiency and/or energy reserve in CHF, and as such may relate to enhanced survival. Therefore, a mild increase in BMI might not be considered an adverse risk factor in CHF, and as such we would be most grateful if Osman et al. (1) could comment on this based on the data from their study. Obesity, and in particular fat mass, has primarily been considered to relate to an unfavorable atherogenic lipoprotein profile, recognized as one of the major risk factors contributing to the development of ischemic heart disease (IHD). Whereas patients with IHD are metabolically stable, patients with CHF can develop substantial catabolism (4).

In view of this, we have hypothesized that low serum cholesterol may be associated with impaired prognosis in CHF (5). We have clinical data supporting this hypothesis, which has been presented recently (6). A recent study by Horne et al. (7) demonstrated that total cholesterol and atherogenic lipid indices were not predictors of impaired clinical outcome in severe IHD. However, an elevated C-reactive protein (a nonspecific marker of systemic inflammation) and reduced left ventricular ejection fraction (reflecting the presence of CHF) were independently related to mortality. Thus, in this study, systemic inflammation but not lipid levels appear to be linked to increased mortality in CHF. Of note, statin therapy was associated with marked beneficial effects on clinical outcome, independently of lipid levels. These findings together lend support to our hypothesis that, in CHF, higher body fat and serum cholesterol may relate to enhanced survival, and perhaps statins actually exert beneficial effects by mechanisms other than lipid-lowering (5). In addition, they may also increase the turnover of endotoxin-laden lipoproteins in the plasma by inhibiting endogenous cholesterol synthesis. This might then lead to endotoxin elimination, reduced cytokine production and, finally, less systemic immune activation.

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REPLY
We thank Drs. Schmidt and Rauchhaus for their insightful comments and appreciate the opportunity to delineate the issue of body fat and prognosis in chronic heart failure (CHF).

In our investigation (1), obesity (body mass index [BMI] >30 kg/m2) was encountered in 37% of the cohort, with no statistically significant difference in clinical outcome among the obese and nonobese (10% of obese patients reached the end point of death or urgent transplantation compared with 18% of the nonobese patients, p = 0.1). Furthermore, although percent fat was lower in those who reached the primary end point than in
survivors, the differences were marginal but statistically significant (p = 0.02). Additional multivariate analyses of our larger current database reveal a significant correlation between body fat and improved prognosis, with a risk ratio (RR) of 0.95 (p = 0.028). When we divided patients into quartiles of body fat, the lowest quartile had an event rate of 11% compared to 5% in those in the highest quartile, suggesting that weight does indeed appear to predict outcome in chronic heart failure (p < 0.05).

We agree with the authors that loss of body fat, muscle and bone mass in severe CHF represent manifestations of the systemic catabolic nature of the disease process and are markers of neurohormonal and cytotoxic aberrations (2,3). Increased adiposity, nevertheless, should not be considered salutary in heart failure. Body fat beyond normal reported ranges and “metabolic stability” represents an excess burden on an already limited cardiopulmonary system and is associated with decreases in functional capacity, as our cardiopulmonary exercise indices suggest. We also wish to highlight the finding in the authors’ own investigation, which suggested the best survival in the “mildly” obese group (BMI 28 to 32 kg/m²) compared to worse survival on either side of this spectrum (BMI >32, RR 1.5, and BMI <28, RR 1.7) (4).

We read with interest the work of the authors on the relationship of cholesterol and prognosis in heart failure. In an earlier investigation, our group similarly described the association of low serum cholesterol in concert with cardiac performance characteristics as an important independent marker of adverse clinical outcome and need for mechanical ventricular support (5). More recently, we have defined the unique association of low high-density lipoprotein cholesterol with a greater propensity for heart failure hospitalizations and death (6). High density lipoproteins are known to interact with cytokine-induced adhesion cell molecule elucidation and to influence the generation of prostacyclin via cyclo-oxygenase stimulation; both of these pathophysiological events are implicated in the natural history of CHF (7). Thus, the current scientific evidence appears to point toward an important association of inflammation, oxidative stress and lipoprotein metabolism in heart failure. Whether these findings represent an epiphenomenon or therapeutic target remains to be established.

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