the progression of ventricular dysfunction. In patients with severe CAD, production and release of endothelin, angiotensin II and activation of neurohormonal systems lead to direct stimulation of interstitial fibrosis, contributing to the pathophysiology of heart failure (6,7).

Thus, two distinct types of ischemic CMP could be separated: ischemic post-MI CMP and ischemic non–post-MI CMP. These entities have dissimilar prevalence, incidence, natural history and could require a dissimilar therapeutic approach.

Obviously, the majority of ischemic non–post-MI CMP is found among patients with severe CAD, LV dysfunction and congestive heart failure in absence of history of MI. Unfortunately, Felker et al. (1) did not report the proportion of patients with ischemic CMP but without history of MI in their population. It would be of interest to disclose these data.

The main pitfall in the differential diagnosis between ischemic post-MI and non–post-MI cardiomyopathies in the clinical setting is related to cases with silent MI in the past. For clinical research purposes, we propose that patients without a history of MI with severe diffuse CAD on coronary angiography and significant global LV dysfunction in absence of regional wall motion abnormalities and/or scars on echocardiography should be considered as bearing ischemic non–post-MI CMP. The recognition of this entity as a different type of ischemic CMP is important for clinical trials and population-based studies aiming to determinate the prevalence, natural history and optimal therapeutic strategies for patients with ischemic non–post-MI CMP.

Alexander Tenenbaum, MD, PhD
Enrique Z. Fisman, MD
Michael Motro, MD
Cardiac Rehabilitation Institute
Chaim Sheba Medical Center
Tel-Hashomet 52621
Israel
E-mail: altenen@yahoo.com

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REPLY

We appreciate the interest of Drs. Tenenbaum, Fisman and Motro in our study (1). We agree that there are likely to be important subsets within the group of patients with ischemic cardiomyopathy (CMP). As they point out, the characteristics and prognosis of patients with heart failure as the result of myocardial infarction (MI) may be different from patients with ischemic CMP and no previous MI. We concur with their assertion that patients with ischemic CMP and no prior MI are more likely to have hibernating myocardium, leading to progressive neurohormonal activation and myocyte apoptosis if coronary blood flow is not restored.

In response to their inquiry, we reassessed our data to determine the proportions of patients in the ischemic etiology group with and without a history of previous MI. Sixty percent of the patients classified as ischemic using our criteria had a prior MI. Compared to patients in the ischemic group without prior MI, the MI group had a significantly better unadjusted survival (49% vs. 32% at five years, $p = 0.001$). Survival for both groups was significantly worse than that of the nonischemic patients (unadjusted survival of 60% at five years). When history of MI was added to the multivariable Cox proportional hazards model to adjust for other differences between the groups, it had a protective effect with a hazard ratio of 0.72 ($p = 0.001$).

One potential explanation for the seemingly paradoxical "protective effect" of a prior MI in patients with coronary artery disease (CAD) and heart failure may relate to differences in the type of coronary disease between the two groups. Even controlling for the extent of CAD using the number of diseased vessels or the CAD index cannot completely adjust for differences in the nature of the CAD (focal vs. diffuse) and the likelihood and completeness of revascularization. We hypothesize that patients with "ischemic non–post-MI CMP" would be more likely to have diffuse coronary disease not readily amenable to traditional revascularization techniques, potentially explaining their worse outcomes. The upcoming STICH trial may shed further light on the efficacy of various surgical therapies in different subgroups of patients with heart failure and CAD.

G. Michael Felker, MD
Linda K. Shaw, MS
Christopher M. O'Connor, MD
Duke University Medical Center
Box 31185
Durham, North Carolina 27710
E-mail: felke001@mc.duke.edu

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