CORRESPONDENCE

Diastolic Heart Failure

TO THE EDITOR: Zile et al. (May 6 issue)[1] conclude that heart failure develops in patients with a normal ejection fraction because of abnormal active and passive diastolic function. However, the applicability of this conclusion to all such patients is uncertain for several reasons. First, accurate assessment of left ventricular volume, on which the conclusions critically depend, requires a three-dimensional imaging technique that measures the long axis[2,3]; two-dimensional techniques are inadequate for this purpose. Second, the majority of the patients studied were men, and on average, they were less than 60 years of age. However, most patients with a normal ejection fraction in whom heart failure develops are elderly women.[4] Third, although the underlying disease in patients with heart failure and a normal ejection fraction differs according to whether hypertension is or is not present, data from these two groups were pooled, precluding the identification of different pathophysiological mechanisms. Fourth, the results do not account for data already in the literature showing that there are rightward, downward shifts of the diastolic pressure–volume relation in some patients with heart failure and a normal ejection fraction.[5] Therefore, the conclusions reached by Zile et al. may not apply to most patients with heart failure and a normal ejection fraction. The mechanisms responsible for this disorder in most patients still need to be elucidated.

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TO THE EDITOR: The conclusions of Zile et al. concerning the pathophysiology of diastolic heart failure are based on the assumption that they have accurately measured ventricular volume. This assumption is unwarranted. Many articles document the inaccuracy and variability of two-dimensional echocardiography and show that three-dimensional methods are superior. My colleagues and I have published measurements of ventricular volume obtained from 18 hypertensive patients with diastolic heart failure and hypertrophy[1] and have shown that although their chordal dimensions are normal according to two-dimensional echocardiography, their end-diastolic volumes on three-dimensional

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echocardiography[2] are significantly greater than those of normal controls (by 39 ml, a 42 percent difference). Thus, the end-diastolic pressure–volume relation is shifted to the right (indicating increased volume), contrary to the findings presented by Zile et al. Because they have a normal ejection fraction, they also have increased stroke volume — a feature consistent with the known pathophysiology of hypertensive disease (which involves salt and fluid retention and excess circulating or central volume) and not consistent with that of true diastolic heart failure in the setting of normal blood pressure (which involves a normal volume and stiff myocardium). Hypertensive patients with diastolic heart failure have volume-overload heart failure. They do not have heart failure involving normal volume and impaired filling, as do normotensive patients with diastolic heart failure. Zile et al. have conflated two conditions with distinct pathophysiological mechanisms.

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TO THE EDITOR: In her Perspective article, Redfield does not recognize the potential role of decreased kidney function in the pathogenesis of diastolic heart failure.[1] The patients described by Zile et al. were relatively young, and these investigators' findings may not reflect the characteristics of diastolic heart failure in the elderly. Older patients with heart failure often have decreased kidney function, and they most frequently present with heart failure due to presumed diastolic dysfunction.[2] Diastolic dysfunction is also frequently accompanied by diabetes and hypertension, which are major risk factors for kidney disease.[3] McAlister et al. found, in a large population of patients with heart failure, that those with decreased kidney function were older and more often had normal cardiac function than those with normal kidney function.[4] This finding suggests that patients with presumed diastolic heart failure may indeed have underlying kidney disease, which results in sodium retention, contributing to the development of heart failure. Clinicians must be aware that abnormal kidney function may be associated with the development of diastolic heart failure, particularly in elderly persons.

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THE AUTHORS REPLY: Maurer et al. suggest that accurate assessment of left ventricular volume requires three-dimensional imaging techniques and that two-dimensional echocardiography is inadequate. This criticism challenges the veracity of virtually every previously reported study involving the use of two-dimensional echocardiography. Citing data from 18 patients, King suggests that left ventricular end-diastolic volume calculated by three-dimensional echocardiography is 42 percent greater in patients with diastolic heart failure than it is in normal controls. We disagree with both Maurer et al. and King. First, our volumetric data are consonant with data from other published studies of diastolic heart failure in which either two-dimensional echocardiography or three-dimensional magnetic resonance imaging techniques were used. Second, even if our study underestimated diastolic volumes by as much as 40 percent, the left ventricular chamber stiffness constant (β) would still be substantially higher in patients with diastolic heart failure than the value in controls. To prove this, we recalculated β, assuming that the volumes in our patients had increased by 40 percent; the mean ($\pm$SD) β value was 0.012±0.01 in the controls, as compared with 0.024±0.01 in the patients with diastolic heart failure ($P<0.001$). Thus, left ventric-

ular diastolic pressure is higher and the left ventricular stiffness constant significantly greater in patients with diastolic heart failure than in controls.

Epidemiologic studies do not suggest that diastolic heart failure is seen only in women older than 75 years of age. Although the prevalence increases with age, diastolic heart failure develops in both men and women in the middle and advanced age groups. Independent of demographic issues, a unique feature of our study was that all patients fulfilled the diagnostic criteria for diastolic heart failure proposed by Vasan and Levy[1] and the European Study Group on Diastolic Heart Failure.[2] Moreover, all our patients had one or more measurements of abnormal active relaxation and passive stiffness, as did those we described in a previous report.[3] Because women generally have more robust hypertrophy than men, it can be expected that left ventricular stiffness would be even higher if the cohort studied consisted predominantly of women of advanced age. Therefore, our data may well underestimate the severity of diastolic dysfunction that is seen in older women with diastolic heart failure.

The "data already in the literature" to which Maurer et al. refer appear in an editorial[4] in which pressure–volume data from four selected patients were reconstructed from data reported by others. This information certainly cannot be considered definitive because data from these four patients do not necessarily fulfill published diagnostic criteria for diastolic heart failure and, as the authors themselves suggest, "knowledge of patient age, sex, and body size" was not available.

We agree with Grieff that many vascular and noncardiac factors (such as renal insufficiency and anemia) may act as precipitants of heart failure in patients with left ventricular dysfunction.

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DR. REDFIELD REPLIES: The role of altered renal function in the pathophysiology of diastolic heart failure deserves further study. In my Perspective article, I emphasize that renal dysfunction contributes to the progression of systolic heart failure and that characteristic renal profiles in diastolic heart failure had not been defined. Studies suggest that the prevalence of renal dysfunction in patients with systolic heart failure is similar to that in patients with diastolic heart failure.[1] However, one study did not show that worsening renal function was a common precipitant of diastolic heart failure.[2] Some authorities argue that volume retention (which can occur with renal dysfunction), may explain the elevated filling pressures observed in patients with diastolic heart failure in the absence of increased ventricular diastolic stiffness; they contend that conventional assessment of left ventricular volumes may not be sensitive enough to detect such changes. The study by Zile et al. does provide extensive data to refute this hypothesis, but clearly, additional studies are needed. Furthermore, as I emphasize in my Perspective article, substantial heterogeneity may exist among patients with diastolic heart failure, with renal dysfunction playing a greater or lesser role in various subgroups of these patients.

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