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Diastolic Heart Failure — A Common and Lethal Condition by Any Name

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This issue of the *Journal* contains two provocative contributions to the literature on heart failure. Owan et al.[1] describe the epidemiologic outcomes and survival rates among patients with heart failure who were admitted to the Mayo Clinic Hospitals for the disease from 1987 through 2001, extending results published in 1998[2]; Bhatia et al.[3] review the shorter-term outcomes among patients hospitalized for heart failure in the province of Ontario over a two-year period, beginning in April 1999. Both groups of investigators subdivided their patients according to the level of ejection fraction. They then compared the characteristics and clinical courses of the patients with a preserved ejection fraction of 50 percent or greater (Owan et al.) or more than 50 percent (Bhatia et al.) to those with a reduced ejection fraction.

Owan et al. and Bhatia et al. use the term "heart failure with preserved ejection fraction," as opposed to the term "diastolic heart failure." Strictly speaking, "heart failure with preserved (or normal) ejection fraction" is not incorrect and appears to be preferred by the American College of Cardiology and the American Heart Association.[4] However, "diastolic heart failure" describes the dominant underlying pathophysiological features[5,6] and has connotations familiar to the clinician. Furthermore, virtually all patients with heart failure and preserved ejection fraction who are studied carefully will show abnormalities in diastolic function and elevated left-ventricular filling pressures.[7] The two current studies remind us that ejection fraction is not a good predictor of clinical disability and suggest that congestive symptoms are more closely related to the filling (diastolic) properties of the ventricle than to the ejection (systolic) properties. Accordingly, the terms "diastolic" and "systolic" heart failure are used here instead of heart failure with "preserved" or "reduced" ejection fractions, respectively.

A principal conclusion of these studies may come as a surprise: patients with diastolic heart failure have the same or only slightly better rates of survival than those with systolic heart failure at one year[1,3] and at five years.[1] These data challenge the widely held perception that the survival rate among patients with most forms of heart disease is inversely related to the ejection fraction, at least for ejection fractions below 45 percent.[8-10] How do we reconcile the findings of Owan et al. and Bhatia et al. with the apparently contradictory results from previous studies, such as the Cardiovascular Health Study (a large, multicenter community-based study)[9] or the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) study (to our knowledge, the only large, randomized clinical trial of the treatment of diastolic heart failure published to date)?[10]

One may start by asking whether the patients in the two current studies could have been misclassified according to ejection fraction. Although there is not complete unanimity on what is the lower limit of normal, 50 percent is reasonable.[5] In the study by Owan et al., the mean (±SD) ejection fraction was 29±10 percent among patients with systolic heart failure and 61±7 percent among

patients with diastolic heart failure; this difference suggests that substantial overlap between the two subgroups was unlikely. (The data of Bhatia et al. are even more clear-cut on this point, since patients with an intermediate ejection fraction [40 to 50 percent] were a separate subgroup.) Furthermore, thanks to studies that involve serial echocardiography, we now know that the ejection fraction does not typically change appreciably between hospital admission and hospital discharge, despite dramatic changes in patients' clinical status.[11] Therefore, the incorrect classification of patients according to their ejection fraction is unlikely.

In my judgment, the difference between the current results and those of previously published studies relates both to patient characteristics and to the growing recognition of diastolic heart failure. It may be important that Owan et al. studied only patients who survived long enough to be discharged from the hospital. As a result, a higher rate of in-hospital mortality among patients with systolic heart failure than among those with diastolic heart failure may have been overlooked in this study. Furthermore, in both studies, the mean age was higher among patients with diastolic heart failure than among those with systolic heart failure. An older population is more likely to have important coexisting medical conditions, such as cerebrovascular disease or renal insufficiency. Since the primary outcome was death from any cause rather than death from cardiac causes, it seems reasonable to postulate that older patients with diastolic heart failure would have been more likely to have complications from these coexisting medical conditions, despite the authors' attempts at statistical adjustment. Unfortunately, the comparison of these results with those of the CHARM study is bedeviled by what are undoubtedly significant differences in the mean age (which was likely to have been higher in the current studies) and the prevalence of severe coronary artery disease (which was likely to have been higher in the CHARM study).

Although the current analyses were carefully performed, one must be cautious in extrapolating the results. First, the population studied by Owan et al. is more than 97 percent white, and no data on ethnic background were given by Bhatia et al. Second, the authors studied the first or only hospitalization for heart failure. The study populations therefore may not reflect the patients who are hospitalized for heart failure in clinical practice, many of whom are admitted repeatedly for exacerbations of the disease or even for procedure-related heart failure. Finally, the study data may not be applicable to outpatients with heart failure.

Another principal conclusion of Owan et al. is that diastolic heart failure has increased in prevalence over time.[1] The authors estimate that, in their study, more than half of the patients discharged with heart failure had diastolic heart failure, and they enumerate the probable explanations. One is the increasing percentage of older patients in the population, coupled with the fact that the prevalence of diastolic heart failure varies directly with the mean age of the population.[6] I concur with the authors' observation that, owing to increasing awareness, clinicians were more likely to admit a patient to the hospital for diastolic heart failure in 2001 than previously. In fact, a systematic search of the literature for "diastolic heart failure" (and related terms) shows an increase in the number of publications by a factor of 20 between 1986 and 2002, which includes the study period of Owan et al. There was similar growth during that period in the number of publications with "diastolic dysfunction" in the title, a relative rarity in 1986. Although not mentioned by Owan et al., the growing availability of echocardiography, as well as point-of-care biomarkers such as brain natriuretic peptide, probably increases the likelihood that patients with dyspnea will be diagnosed as having diastolic heart failure, whether or not they are admitted to the hospital.

The nosology of heart failure has been the subject of much current debate, and some extreme positions have been taken. The observation that 22 to 29 percent of patients with diastolic heart failure die within one year of hospital discharge, and 65 percent die within five years, is a reminder that we are facing a lethal condition, regardless of its name. Owan et al. also show that, in recent years, there has been little improvement in survival rate among patients with diastolic heart failure, in contrast to the improvement in survival rate over time among patients with systolic heart failure.

The news is not all bad, however. The noted improvement in the survival rate of patients with systolic heart failure[1] provides encouragement that emerging treatment strategies for diastolic

heart failure, such as the use of angiotensin-receptor blockers,[12,13] might eventually have a clinical effect. We should also not neglect preventive measures with proven efficacy (such as antihypertensive therapy),[14] given that there is no effective cure for aging. The prevention of a first or recurrent myocardial infarction is likely to be the best means we have to keep the ejection fraction "preserved." However, the development of specific, effective management approaches for diastolic heart failure must also become a high priority.

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Women in Academic Medicine — Progress and Challenges

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In 1960, only about 5 percent of medical students in the United States were women; today, the numbers of women and men in medical school are approximately equal. This apparent success story, however, is tempered by observations that women who enter academic medicine have been less likely than men to be promoted or to serve in leadership positions.[1] As of 2005, only 15 percent of full professors and 11 percent of department chairs were women.[2]

In this issue of the *Journal*, Jagsi et al.[3] document similar trends for women as authors of articles in prominent medical journals. They report that nearly five times as many women authored original articles published in six major journals in 2004 than in 1970. Despite this progress, in 2004 small proportions of first and senior (last listed) authors were women (29.3 percent and 19.3 percent, respectively). Percentages of female authors were highest in those journals focused on pediatrics and obstetrics and gynecology — fields in which women compose a larger proportion of faculty members overall. In 2004, rates of female authorship were likewise low for guest editorials in two general medical journals (this journal and *JAMA*). As Jagsi and colleagues point out, invited editorialists and senior authors of original articles are typically more senior faculty members; the same may be true of first authors of articles in the high-impact journals included in this study. The authorship gap is likely to narrow substantially only when more women reach senior faculty positions.

What accounts for the apparent paradox of dramatic growth in the rate of women entering the field of medicine and the achievement of less