Burden of Systolic and Diastolic Ventricular Dysfunction in the Community
Appreciating the Scope of the Heart Failure Epidemic

Margaret M. Redfield, MD

Steven J. Jacobsen, MD, PhD

John C. Burnett, Jr, MD

Douglas W. Mahoney, MS

Kent R. Bailey, PhD

Richard J. Rodeheffer, MD

CONGESTIVE HEART FAILURE (CHF) is a clinical syndrome defined by characteristic symptoms and physical findings. Echocardiography is often performed in patients with CHF to measure the ejection fraction (EF) and determine if systolic function is reduced, systolic CHF or preserved, diastolic CHF. Comprehensive Doppler echocardiography can now characterize diastolic function directly in addition to measurement of the EF.

Cardiovascular diseases (CVDs) such as hypertension, coronary artery disease, and cardiomyopathies often lead to systolic and diastolic ventricular dysfunction. Nearly all patients with systolic dysfunction have some degree of concomitant diastolic dysfunction, specifically, impaired relaxation and variable decreases in ventricular compliance.[1] However, it is now recognized that patients with normal EF can display marked impairment in diastolic function (isolated diastolic dysfunction).[2]

Clinically, it has been recognized that some patients with advanced systolic dysfunction remain free of symptoms of CHF. Thus, individuals may have systolic dysfunction without receiv-

Context Approximately half of patients with overt congestive heart failure (CHF) have diastolic dysfunction without reduced ejection fraction (EF). Yet, the prevalence of diastolic dysfunction and its relation to systolic dysfunction and CHF in the community remain undefined.

Objectives To determine the prevalence of CHF and preclinical diastolic dysfunction and systolic dysfunction in the community and determine if diastolic dysfunction is predictive of all-cause mortality.

Design, Setting, Participants Cross-sectional survey of 2042 randomly selected residents of Olmsted County, Minnesota, aged 45 years or older from June 1997 through September 2000.

Main Outcome Measures Doppler echocardiographic assessment of systolic and diastolic function. Presence of CHF diagnosis by review of medical records with designation as validated CHF if Framingham criteria are satisfied. Subjects without a CHF diagnosis but with diastolic or systolic dysfunction were considered as having either preclinical diastolic or preclinical systolic dysfunction.

Results The prevalence of validated CHF was 2.2% (95% confidence interval [CI], 1.6%-2.8%) with 44% having an EF higher than 50%. Overall, 20.8% (95% CI, 19.0%-22.7%) of the population had mild diastolic dysfunction, 6.6% (95% CI, 5.5%-7.8%) had moderate diastolic dysfunction, and 0.7% (95% CI, 0.3%-1.1%) had severe diastolic dysfunction with 5.6% (95% CI, 4.5%-6.7%) of the population having moderate or severe diastolic dysfunction with normal EF. The prevalence of any systolic dysfunction (EF ≤50%) was 6.0% (95% CI, 5.0%-7.1%) with moderate or severe systolic dysfunction (EF ≤40%) being present in 2.0% (95% CI, 1.4%-2.5%). CHF was much more common among those with systolic or diastolic dysfunction than in those with normal ventricular function. However, even among those with moderate or severe diastolic or systolic dysfunction, less than half had recognized CHF. In multivariate analysis, controlling for age, sex, and EF, mild diastolic dysfunction (hazard ratio, 8.31 [95% CI, 3.00-23.1], P<.001) and moderate or severe diastolic dysfunction (hazard ratio, 10.17 [95% CI, 3.28-31.0], P<.001) were predictive of all-cause mortality.

Conclusions In the community, systolic dysfunction is frequently present in individuals without recognized CHF. Furthermore, diastolic dysfunction as rigorously defined by comprehensive Doppler techniques is common, often not accompanied by recognized CHF, and associated with marked increases in all-cause mortality.
JAMA. 2003;289:194-202 www.jama.com

Author Affiliations: Division of Cardiovascular Diseases, Department of Internal Medicine (Drs Redfield, Burnett, and Rodeheffer) and the Divisions of Clinical Epidemiology (Dr Jacobsen) and Biostatistics (Mr Mahoney and Dr Bailey), and Department of Health Science Research, Mayo Clinic and Foundation, Rochester, Minn.
Corresponding Author and Reprints: Margaret M. Redfield, MD, Guggenheim 9, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (e-mail: redfield.margaret @mayo.edu).

ing a diagnosis of or treatment for CHF. This has been termed *preclinical systolic dysfunction* and may be common.[3-5] However, the prevalence of diastolic dysfunction and its relation to systolic dysfunction and recognized CHF in the community is unclear.

The efficacy of therapy to abort or delay the progression of preclinical systolic dysfunction to CHF is recognized by CHF practice guidelines.[6] Studies indicate that even simple Doppler evidence of diastolic dysfunction is an independent risk factor for the future development of CHF and cardiac death.[7,8] Thus, if common, early recognition and treatment of preclinical systolic and diastolic dysfunction represent a potentially powerful strategy to reduce the incidence of CHF.

Our objective was to establish the prevalence of preclinical systolic and diastolic dysfunction and the prevalence of CHF in randomly selected residents of Olmsted County, Minnesota,[3] aged 45 years or older. Furthermore, we sought to determine whether the presence of diastolic dysfunction is independently predictive of all-cause mortality.

METHODS

In 1990, 96% of the 106 470 residents of Olmsted County were white. Other characteristics of this population have been previously described.[9-11] The Mayo Foundation institutional review board approved this study.

Using the resources of the Rochester Epidemiology Project,[10] a random sample of residents who were at least 45 years old as of January 1, 1997, was identified. Participants were enrolled and studied during a 3-year period, ending September 30, 2000. Of the 4203 eligible residents invited, 2042 (47%) participated. Analysis of the medical records of 500 randomly selected residents who did not participate revealed similar age and sex distribution to that observed in participants and a similar prevalence of hypertension, coronary artery disease, previous myocardial infarction, diabetes, previous cardiovascular hospitalization, and CHF.

Box. Framingham Criteria for the Clinical Diagnosis of Congestive Heart Failure[9]

Major Criteria
Paroxysmal nocturnal dyspnea
Orthopnea
Elevated jugular venous pressure
Pulmonary rales
Third heart sound
Cardiomegaly on chest radiograph
Pulmonary edema on chest radiograph

Minor Criteria
Peripheral edema
Night cough
Dyspnea on exertion
Hepatomegaly
Pleural effusion
Heart rate >120/min
Weight loss ≥4.5 kg in 5 days*

*Weight loss ≥4.5 kg in 5 days is considered a major criterion if it occurred in response to therapy for congestive heart failure (CHF). A patient was considered to have validated CHF if 2 major criteria were present or 1 major and 2 minor criteria were present concurrently.

Community medical records for each participant were reviewed by trained nurse abstractors using established criteria for hypertension[12] or myocardial infarction.[13] In addition, clinical diagnoses of coronary artery disease and diabetes mellitus were recorded. Each participant underwent a focused physical examination that included measurement of blood pressure, height, and weight. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Each participant's medical records were reviewed to determine if any diagnosis of CHF had been made. If so, each medical encounter was reviewed to determine whether the documented clinical information fulfilled Framingham criteria[9] (validated CHF; Box). Participants with no CHF diagnosis but with either diastolic or systolic dysfunction at echocardiography were considered to have preclinical diastolic or systolic dysfunction. Such designation does not imply that the participant would definitely develop CHF or did not have symptoms, only that the participant had not sought evaluation or had not had an evaluation that resulted in a diagnosis of CHF.

Doppler Echocardiography

All echocardiograms were performed by 1 of 3 registered diagnostic cardiac sonographers who used the same echocardiographic instrument (HP-2500, Palo Alto, Calif) according to a standardized protocol and interpreted by a single echocardiologist (M.M.R.) who was masked to clinical data. Two-dimensional (2-D) and color Doppler imaging were performed to screen for valvular disease.

In each participant, measurement of EF was performed by M-mode echocardiography using the modified Quinones formula, by the quantitative 2-D (biplane Simpson) method, and by the semiquantitative 2-D visual estimate method.[11,14-17]

Each participant underwent pulsed-wave Doppler examination of mitral inflow before and during Valsalva maneuver and of pulmonary venous inflow and Doppler tissue imaging of the mitral annulus. Diastolic function was categorized according to the progression of diastolic dysfunction: normal; *mild*, defined as impaired relaxation without evidence of increased filling pressures; *moderate*, defined as impaired

relaxation associated with moderate elevation of filling pressures or pseudonormal filling, and *severe*, defined as advanced reduction in compliance or reversible or fixed restrictive filling as previously described and validated (**FIGURE 1**).[1,18] Participants were re-

quired to have 2 Doppler criteria consistent with moderate or severe diastolic dysfunction to be so classified. Subjects with 1 criterion for moderate or severe diastolic dysfunction or those whose parameters were borderline and suggestive of but not definitive for di-

astolic dysfunction were classified as indeterminate rather than as normal.

Left ventricular mass and left atrial volume were calculated from M-mode and 2-D measurements, respectively, and were indexed to body surface area as previously described.[19,20]

Figure 1. Doppler Criteria for Classification of Diastolic Function
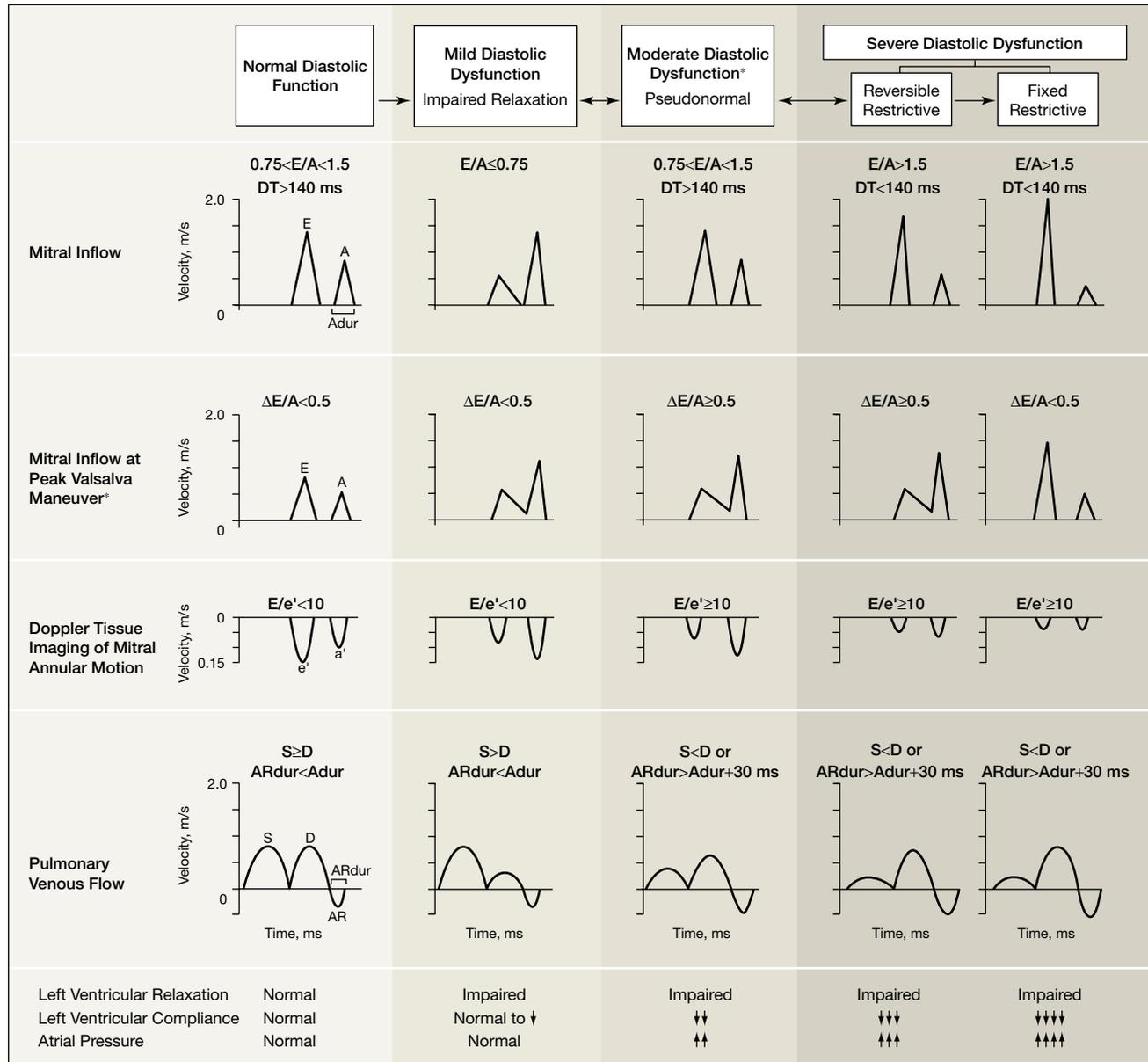
Participants with atrial fibrillation with DT >140 ms, other arrhythmia, fusion of E and A, or in whom diastolic parameters were not obtained, who had only 1 criterion suggesting moderate or severe diastolic dysfunction, or in whom diastolic parameters were borderline and suggestive of but not diagnostic of abnormality were classified as having indeterminate diastolic function. E, peak early filling velocity; A, velocity at atrial contraction; DT, deceleration time; Adur, A duration; ARdur, AR duration; S, systolic forward flow; D, diastolic forward flow; AR, pulmonary venous atrial reversal flow; e', velocity of mitral annulus early diastolic motion; a', velocity of mitral annulus motion with atrial systole; DT, mitral E velocity deceleration time.
  *Corrected for E/A fusion.[40]

As part of the Rochester Epidemiology Project infrastructure, mortality data on Olmsted County residents are routinely collected by reviewing community medical records, death certificates, and obituary notices. Participants were followed up until death or October 1, 2002, at which time they were censored. This provided 7000 person-years of follow-up, with a median (25th, 75th percentile) of 3.5 (2.9, 4.2) person-years of follow-up. Active surveillance of the first 41% (n=974) of the cohort recruited to participate in our study for a follow-up visit identified no additional deaths to those identified via the above mechanisms.

Statistical Methods

For each EF method, the corresponding distribution was summarized as the empirically estimated cumulative distribution function. The overall prevalence of systolic dysfunction was estimated for each method among participants from whom EF was obtained by that method with the corresponding 95% confidence interval (CI) based on the exact binomial distribution. Similar methods were used to estimate the overall prevalence of diastolic dysfunction. The association between the prevalence of systolic dysfunction with clinical variables was investigated using the χ^2 test for univariate associations and logistic regression when controlling for potential confounding variables. The Mantel-Haenszel χ^2 test of trend was used to investigate the association between the ordinal scale of diastolic dysfunction with dichotomous clinical variables and the Spearman correlation coefficient for continuous variables. Ordinal logistic regression was used to adjust the association of clinical variables with diastolic dysfunction for age and sex. The survival-free (of any cause) status was estimated using the Kaplan-Meier method and the association with diastolic dysfunction was assessed using the log-rank test. The Cox proportional hazards regression model was used to adjust the association of diastolic dysfunction with all-cause mortality for age, sex, and EF. The proportional hazards assumption was evaluated and not rejected using methods developed by Grambsch and Therneau.[21] All analyses were done using SAS version 8 (SAS Institute, Cary, NC) except for the test of proportional hazards which was done using the survival analysis software in S-Plus Version 6.1.2 (Seattle, Wash).

RESULTS

Study Participants

The mean (SD) age of study participants was 62.8 (10.6) with 29.4% aged 45 through 54, 30.6% aged 55 through 64, 25.4% aged 65 through 74 years, and 14.6% aged 75 years or older. The mean (SD) BMI was 28.4 (5.41). Of the participants, 8.9% were current and 50.1% were former smokers, 4.5 had diabetes, 12.2% had a history of coronary artery disease, and 4.8% had a previous myocardial infarction.

Congestive Heart Failure

The prevalence of any CHF diagnosis was 2.6% (95% CI, 1.9%-3.3%) with 21 participants (41%) having an EF higher than 50%. A validated diagnosis of CHF was present in 45 participants (2.2%; 95% CI, 1.6%-2.8%) with 20 (44%) of those having an EF higher than 50%. The mean (SD) time between CHF diagnosis and the echocardiogram was 4.9 (4.1) years (range, 0.1-16.2 years). The prevalence of validated CHF increased with age groups: 0.7% for those aged 45 through 54; 1.3% in those aged 55 through 64; 1.5% for those aged 65 through 74; and 8.4% for those aged 75 years or older. The P value with or without adjustment for sex was $P<.001$. The prevalence of validated CHF was 2.7% in men vs 1.7% in women ($P=.11$, without adjustment for age). When adjusted for age, CHF was slightly more common in men ($P=.03$).

Diastolic Dysfunction

Diastolic function was classified as normal or abnormal in 1779 participants (87.1%) and as indeterminate in 263 participants (12.9%). Among the 45 with

Table 1. Prevalence of Systolic and Diastolic Dysfunction According to Age and Sex*

| | No. (%) of Patients Affected | | | | |
| | Age Group, y | | | | |
Variables	45-54	55-64	65-74	≥75	Overall
Diastolic Dysfunction					
Mild					
All	27 (4.8)	72 (13.2)	149 (34.2)	123 (52.8)	371 (20.8)
Men	20 (7.2)	43 (16.0)	76 (37.2)	49 (57.0)	188 (22.5)
Women	7 (2.4)	29 (10.4)	73 (31.6)	74 (50.3)	183 (19.4)
Moderate					
All	8 (1.4)	33 (6.0)	43 (9.9)	34 (14.6)	118 (6.6)
Men	5 (1.8)	19 (7.1)	17 (8.3)	15 (17.4)	56 (6.7)
Women	3 (1.0)	14 (5.0)	26 (11.3)	19 (12.9)	62 (6.6)
Severe					
All	0 (0)	2 (0.4)	3 (0.7)	8 (3.4)	13 (0.7)
Men	0 (0)	0 (0)	2 (1.0)	3 (3.5)	5 (0.6)
Women	0 (0)	2 (0.7)	1 (0.4)	5 (3.4)	8 (0.8)
Systolic Dysfunction					
Any, ejection fraction ≤50%					
All	18 (3.0)	30 (4.8)	37 (7.1)	38 (12.9)	123 (6.0)
Men	15 (5.1)	23 (7.4)	27 (10.6)	26 (22.8)	91 (10.2)
Women	3 (1.0)	7 (2.2)	10 (3.8)	12 (6.6)	32 (3.8)
Moderate to severe, ejection fraction ≤40%					
All	5 (0.8)	8 (1.3)	14 (2.7)	13 (4.4)	40 (2.0)
Men	5 (1.7)	6 (1.9)	12 (4.7)	9 (7.9)	32 (3.6)
Women	0 (0.0)	2 (0.6)	2 (0.8)	4 (2.2)	8 (1.0)

*A total of 1799 participants were classified as having normal diastolic function or as having mild, moderate, or severe diastolic dysfunction with 243 classified as indeterminate. Ejection fraction was assessed in 2036 participants.

Table 2. Association of Diastolic Function With Clinical Parameters

	No. (%) of Participants				
		Diastolic Dysfunction			
Variables	Normal	Mild	Moderate	Severe	P Value
Men	587 (70.2)	188 (22.5)	56 (6.7)	5 (0.6)	.40
Women	690 (73.2)	183 (19.4)	62 (6.6)	8 (0.8)	
Age, y					
45-64	969 (87.2)	99 (8.9)	41 (3.7)	2 (0.2)	.001
≥65	308 (46.1)	272 (40.7)	77 (11.5)	11 (1.6)	
Ejection fraction, %*					
>50	1259 (74.5)	331 (19.6)	95 (5.6)	5 (0.3)	.001
≤50	18 (20.5)	39 (44.3)	23 (26.1)	8 (9.1)	
Hypertension					
No	1013 (79.3)	198 (15.5)	62 (4.9)	5 (0.4)	.001
Yes	264 (52.7)	173 (34.5)	56 (11.2)	8 (1.6)	
Diabetes					
No	1211 (73.3)	323 (19.5)	108 (6.5)	11 (0.7)	.001
Yes	66 (52.4)	48 (38.1)	10 (7.9)	2 (1.6)	
Coronary disease					
No	1197 (75.3)	304 (19.1)	84 (5.3)	5 (0.3)	.001
Yes	80 (42.3)	67 (35.4)	34 (18.0)	8 (4.2)	
Myocardial infarction					
No	1250 (73.4)	339 (19.9)	106 (6.2)	8 (0.5)	.001
Yes	27 (35.5)	32 (42.1)	12 (15.8)	5 (6.6)	
Validated CHF diagnosis					
No	1276 (72.6)	362 (20.6)	112 (6.4)	7 (0.4)	.001
Yes	1 (4.5)	9 (40.9)	6 (27.3)	6 (27.3)	
CHF diagnosis					
No	1276 (72.8)	358 (20.4)	111 (6.3)	7 (0.4)	.001
Yes	1 (3.7)	13 (48.2)	7 (25.9)	6 (22.2)	
Body mass index, kg/m²					
<25	344 (75.1)	74 (16.2)	35 (7.6)	5 (1.1)	
25-30	546 (72.6)	153 (20.3)	48 (6.4)	5 (0.7)	.03
≥30	387 (68.0)	144 (25.3)	35 (6.2)	3 (0.5)	

Abbreviation: CHF, congestive heart failure. Percentages may not sum to 100 due to rounding.
*In 1 patient, it was possible to assess diastolic dysfunction but not ejection fraction.

validated CHF, only 1 met Doppler criteria for normal diastolic function. Twenty-one met Doppler criteria for diastolic dysfunction. The remaining 23 participants were classified as indeterminate, 13 for atrial fibrillation with mitral inflow deceleration time greater than 140 milliseconds, 1 for other atrial arrhythmia, 1 for mild mitral stenosis, 3 for E–A fusion, and 5 who had borderline parameters that were suggestive of diastolic dysfunction but did not meet all criteria required for designation as diastolic dysfunction.

Overall, 20.8% (95% CI, 19.0%-22.7%) had mild, 6.6% (95% CI, 5.5%-7.8%) had moderate, and 0.7% (95% CI, 0.3%-1.1%) had severe diastolic dysfunction (Table 1) with 5.6% (95% CI, 4.5%-6.7%) having moderate or severe

diastolic dysfunction with normal EF. The prevalence of diastolic dysfunction increased with age, was more common in participants with CVD, diabetes, or systolic dysfunction, and was equally common in men and women (**TABLE 1** and **TABLE 2**). A greater percentage of particpants with mild diastolic dysfunction (38.8%) were obese (BMI >30) compared with those with normal (30.3%) diastolic function or moderate (29.7%) or severe (23.1%) diastolic dysfunction.

Systolic Dysfunction

We obtained EF from 78.0% of participants by M-mode, 79.2% by biplane Simpson method, and 99.7% by 2-D visual methods. Of the 2042 subjects, 1888 (92.5%) had quantitative assess-

ment of EF measured by M-mode or biplane Simpson method if no M-mode was possible. The mean (SD) EF among participants without CD was similar by M-mode (63.5% [6.5%]), biplane Simpson (63.9% [6.7%]), and 2-D visual (63.3% [5.4%]) methods.

The cumulative distribution of EF within the population as assessed by the 3 techniques is displayed in **FIGURE 2**, which illustrates the prevalence of systolic dysfunction according to the EF level and method of measuring it.

In 1888 participants with a quantitative EF assessment, the prevalence was 6.5% (95% CI, 5.4%-7.6%) for those with an EF of 50% or less and was 1.8% (95% CI, 1.2%-2.4%) for those with an EF of 40% or less. Among 2036 participants whose EF was measured by the 2-D visual method, the prevalence was 6.0% (95% CI, 5.0%-7.1%) for those with an EF of 50% or less and was 2.0% (95% CI, 1.4%-2.5%) for those with an EF of 40% or less. The prevalence of systolic dysfunction was lower when restricting the population by using only 1 quantitative method (Figure 2), was higher in men than women (**TABLE 3**) with and without controlling for age (P<.001 for all), and increased with age with and without adjustment for sex (P<.001 for all). Systolic dysfunction determined by the 2-D visual method was more common in participants with CD (Table 3). All associations were similar when only participants with quantitative EF assessment were examined.

Diastolic and Systolic Function Parameters

An EF of 50% or less was present in 1.4% of participants with normal, 10.5% with mild, 19.5% with moderate, 61.5% with severe, and 13.6% with indeterminate diastolic function. Overall, 100 participants (5.6%; 95% CI, 4.5%-6.7%) had moderate or severe diastolic dysfunction but had normal EF (isolated diastolic dysfunction).

Among subjects with normal EF and no CHF diagnosis, increasing severity of diastolic dysfunction was associated with a higher mean (SD) left ven-

tricular mass index (normal, 92.2 [17.7]; mild, 105.9 [24.8]; moderate, 104.4 [25.1]; and severe, 107.6 [44.2] g/m²; Spearman $r=0.23$; $P<.001$) and mean (SD) left atrial volume index (normal, 22.9 [6.0]; mild, 24.6 [7.6]; moderate, 30.5 [8.1]; and severe, 46.3 [12.6] mL/ m²; Spearman $r=0.20$; $P<.001$).

Ventricular Dysfunction and CHF

FIGURE 3 shows the percentage of participants with any or validated CHF diagnosis according to the level of systolic or diastolic dysfunction. The percentage of participants with recognized CHF increased according to the severity of systolic or diastolic dysfunction, clearly indicating that diastolic as well as systolic dysfunction is associated with CHF. However, even when only participants with moderate or severe diastolic dysfunction or with an EF of 40% or less are considered less than half had any or validated CHF diagnosis. Of participants with an EF of 40% or less, 47.5% were taking angiotensin-converting enzyme (ACE) inhibitors and 22.5% were taking β-blockers. Of subjects with moderate or severe diastolic dysfunction, 14.2% were taking ACE inhibitors and 40.2%, β-blockers.

The prevalence of preclinical systolic and diastolic dysfunction in a high-risk group defined by simple clinical characteristics greatly exceeded that observed in the general adult population (TABLE 4).

All-cause mortality (n=48 deaths) was increased among those with diastolic dysfunction (FIGURE 4). Multivariate analysis showed that diastolic dysfunction was predictive of all-cause mortality even when controlling for age, sex, and EF (TABLE 5).

COMMENT

This study provides the first estimates of the prevalence of diastolic dysfunction in the community as assessed by rigorous and hemodynamically validated Doppler criteria. Diastolic dysfunction was common and isolated diastolic dysfunction was as common as systolic dysfunction. The frequency of CHF increased dramatically with increasing severity of

Figure 2. Cumulative Distribution of Ejection Fraction Within the Population
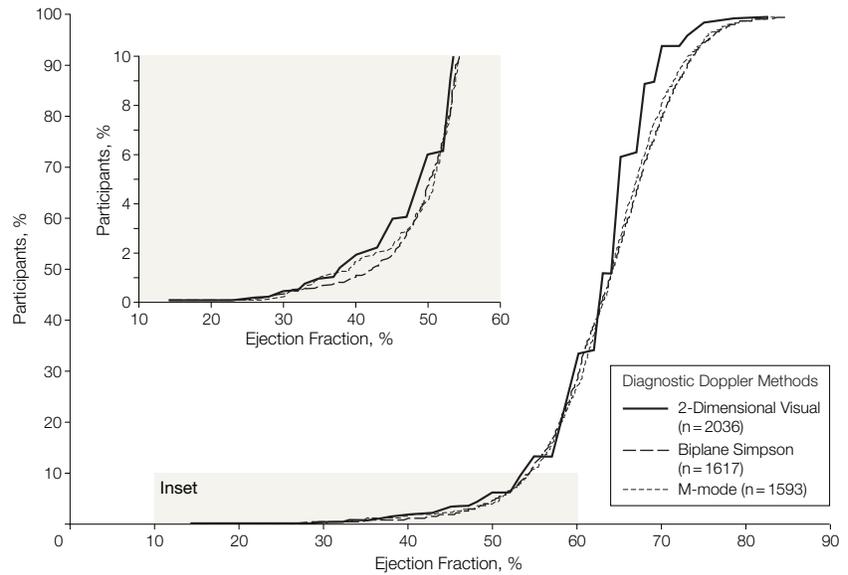
Ejection fraction as assessed by M-mode echocardiography, quantitative 2-dimensional (2-D) echocardiography (biplane Simpson) and semiquantitative 2-D echocardiography.

Table 3. Association of Systolic Dysfunction With Cardiovascular Disease

| | Ejection Fraction, % | | | | |
| | ≤50 | | | ≤40 | |
Variable	No. of Participants at Risk	No. (%) of Participants Affected	P Value	No. (%) Participants Affected	P Value
Hypertension					
No	1440	66 (4.6)	.001	20 (1.4)	.004
Yes	596	57 (9.6)		20 (3.4)	
Diabetes					
No	1885	102 (5.4)	.001	34 (1.8)	.07
Yes	151	21 (13.9)		6 (4.0)	
Coronary disease					
No	1789	71 (4.0)	.001	16 (0.9)	.001
Yes	247	52 (21.0)		24 (9.7)	
Myocardial infarction					
No	1939	98 (5.1)	.001	26 (1.3)	.001
Yes	97	25 (25.8)		14 (14.4)	
Validated CHF diagnosis					
No	1991	98 (4.9)	.001	22 (1.1)	.001
Yes	45	25 (55.6)		18 (40.0)	
CHF diagnosis					
No	1985	93 (4.7)	.001	19 (1.0)	.001
Yes	51	30 (58.8)	.001	21 (41.2)	
Body mass index, kg/m²					
<25	526	25 (4.8)		9 (1.7)	
25-30	857	53 (6.2)	.30	19 (2.2)	.77
≥30	653	45 (6.9)		12 (1.8)	

Abbreviation: CHF, congestive heart failure.

diastolic dysfunction. However, even severe diastolic dysfunction was often preclinical with no recognized CHF diagnosis. When controlling for age, sex, and EF both mild and moderate or severe diastolic dysfunction were predictive of all-cause mortality. Systolic dysfunction was also common. Although the frequency of CHF also increased with worsening systolic function, even among those with an EF of 40% or less, fewer than 50% of participants had a diagnosis of CHF. Simple clinical characteristics allow identification of individuals at highest risk for preclinical diastolic or systolic dysfunction.

A novel aspect of this study is our effort to describe the frequency of diastolic dysfunction and its association with systolic dysfunction and CHF in the population. These data are important because population-based studies[9,22-24] have repeatedly demonstrated that 40% to 50% of individuals with CHF have normal EF, a finding we again confirm. Recent studies have documented that individuals with CHF and normal EF consistently demonstrate diastolic dysfunction when subjected to hemodynamic study and document that patients presenting with CHF and normal EF do not have transient systolic dysfunction.[2,25] Furthermore, using more rudimentary indices to assess diastolic function, Aurigemma et al[7] documented that mitral inflow patterns suggesting mild or moderate or severe diastolic dysfunction were independently predictive of future development of CHF in free-living older volunteers. Bella et al[8] report that a mitral inflow pattern suggestive of diastolic dysfunction was associated with increased cardiac mortality, independent of pertinent covariates. In our study, we used more rigorous Doppler methods to characterize diastolic function, requiring that 2 indices proven as predictive of advanced diastolic dysfunction be present for assignment to the moderate or severe diastolic dysfunction category. We observed the previously described association between diastolic dysfunction and age.[26] These data are consistent with age-associated increases in CVD and with studies suggesting that senescence itself may be associated with impairment in diastolic function.[27] The presence of diastolic dysfunction was closely associated with the presence of CVD, confirming the propensity of hypertension[28,29] and coronary artery disease[28,30] to produce diastolic dysfunction. Even confining the analysis to participants with normal EF and no CHF, worsening diastolic dysfunction was associated with increases in indexed left ventricular mass and left atrial volume. These structural findings support the Doppler evidence of diastolic dysfunction because the hypertrophied ventricle is more likely to display diastolic dysfunction and chronic increases in left atrial pressure associated with diastolic dysfunction would be expected to lead to atrial enlargement. Finally, we demonstrate that, as rigorously defined in our study, both mild and moderate or severe diastolic

Figure 3. Relationship Between Congestive Heart Failure (CHF) Diagnosis and Ventricular Dysfunction
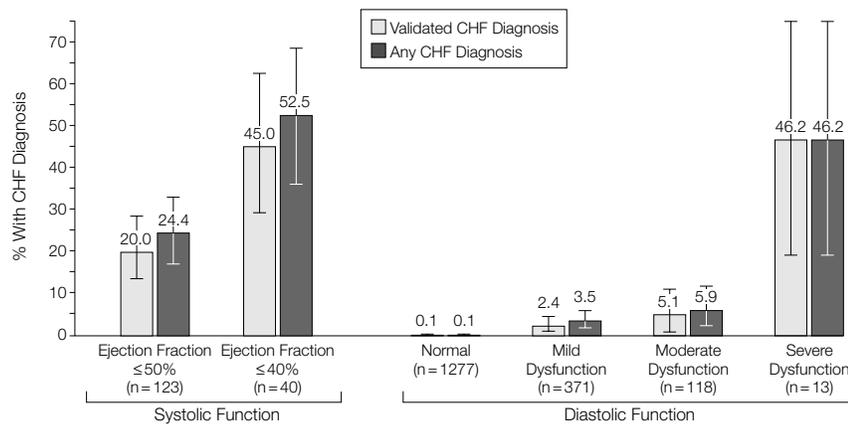
The frequency and 95% confidence intervals of the percentage estimate of any CHF diagnosis or validated CHF diagnosis among participants with systolic or diastolic dysfunction.

Table 4. Prevalence of Preclinical Systolic and Diastolic Dysfunction in the Community*

Variables	No. of Participants	Prevalence (95% Confidence Interval)			
		Ejection Fraction, %		Diastolic Dysfunction	
		≤40	≤50	Mild	Moderate to Severe
General Adult Population					
All	1991	1.1 (0.7-1.7)	4.9 (4.0-6.0)	20.6 (18.7-22.6)	6.8 (5.6-8.0)
Men	952	2.0 (1.2-3.1)	7.9 (6.3-9.8)	22.3 (19.5-25.3)	6.2 (4.7-8.1)
Women	1039	0.3 (0.1-0.8)	2.2 (1.4-3.3)	19.1 (16.7-21.8)	7.3 (5.7-9.1)
High-Risk Population (Age ≥65 y and Hypertension or Coronary Artery Disease)					
All	396	2.8 (1.4-4.9)	10.9 (8.0-14.4)	47.6 (42.1-53.1)	16.5 (12.6-20.9)
Men	196	5.1 (2.5-9.2)	16.8 (11.9-22.8)	48.7 (40.7-56.8)	14.6 (9.5-21.0)
Women	200	0.5 (0.0-2.8)	5.0 (2.4-9.0)	46.5 (38.8-54.3)	18.2 (12.7-24.9)

*Preclinical denotes no previous validated congestive heart failure diagnosis. Ejection fraction was assessed by 2-D visual method.

dysfunction was associated with marked increases in all-cause mortality, independent of age, sex, and EF.

In our study, EF was measured by 3 different techniques to facilitate comparison to previous studies that have used a variety of EF methods. The prevalence of any systolic dysfunction was previously reported as 7.7% for an urban population (aged 25-75 years; biplane Simpson method) in North Glasgow, Scotland.[3] When age, sex, and technique-specific prevalence rates are compared, we found a somewhat lower prevalence of systolic dysfunction in Olmsted County. Devereux et al[31] reported that 14.1% of American Indians (aged 45-74 years) had systolic dysfunction.[31] Other population-based studies have reported prevalence rates similar to ours when age, sex, and technique-specific rates were examined.[4,32] Although the prevalence of systolic dysfunction increased with increasing severity of diastolic dysfunction, most participants with diastolic dysfunction had a normal EF. Indeed, moderate or severe isolated diastolic dysfunction was as common as systolic dysfunction.

The frequency of any and validated CHF diagnoses among patients with ventricular dysfunction increases with the severity of ventricular dysfunction, but even among those with advanced diastolic or systolic dysfunction, more than 50% have no CHF diagnosis or received no treatment. Although previous studies also suggest that up to 50% of patients with systolic dysfunction have preclinical systolic dysfunction,[3-5] the current data extend previous studies by examining both types of ventricular dysfunction known to be associated with the development of CHF, their relation to each other, and the frequency of CHF diagnosis. Easily identified high-risk groups have a higher prevalence of preclinical ventricular dysfunction.

The lifetime risk of developing CHF for those who have reached the age of 40 years is 20% for both men and women[33] and exceeds the lifetime risk of many conditions commonly screened for in the community. Prevention of CHF

Figure 4. Kaplan-Meier Mortality Curves for Participants With Normal Diastolic Function vs Subjects With Mild or Moderate or Severe Diastolic Dysfunction
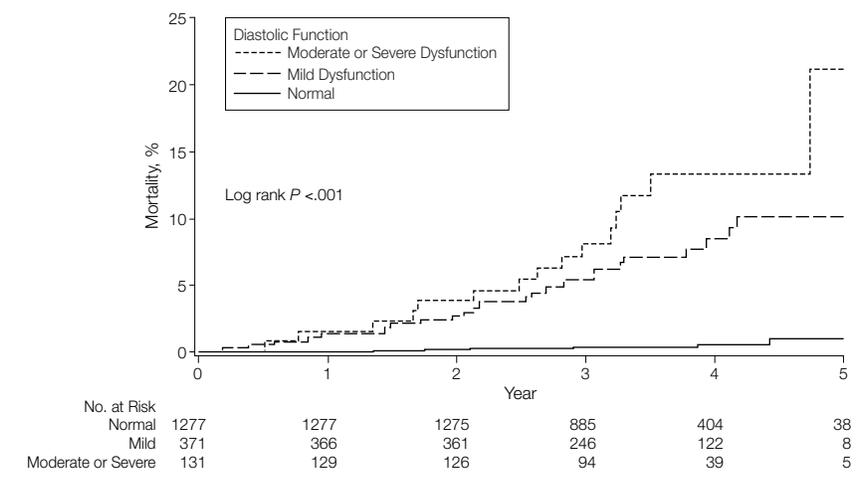
Table 5. Multivariate Analysis of Predictors of All-Cause Mortality

Variables	Hazard Ratio (95% Confidence Interval)	P Value
Age per year	1.06 (1.03-1.10)	.004
Male sex	1.40 (0.74-2.68)	.30
Ejection fraction, per 5 EF % points	0.81 (0.71-0.92)	.02
Mild diastolic dysfunction vs normal diastolic function	8.31 (3.00-23.10)	<.001
Moderate to severe diastolic dysfunction vs normal diastolic function	10.17 (3.28-31.00)	<.001

through the treatment of preclinical systolic dysfunction is recommended in CHF guidelines.[6] Although we acknowledge the lack of therapies proven to modify disease course in diastolic CHF, several clinical trials are underway. The current data are crucial if we are to be poised to extend the paradigm of prevention of CHF through treatment of preclinical systolic dysfunction to those with preclinical diastolic dysfunction. Screening strategies to detect preclinical ventricular dysfunction include Doppler echocardiography and potentially, measurement of plasma brain natriuretic peptide concentration (BNP). However, studies vary as to the sensitivity and specificity of BNP for the detection of systolic or diastolic dysfunction and more data are needed.[11,34-39]

The Olmsted County population is primarily white and may not be representative of national demographics of diastolic and systolic dysfunction. Although comparison of the clinical characteristics of participants and nonparticipants did not reveal significant differences, preferential participation by subjects with or without disease cannot be excluded.

In the community, systolic dysfunction is frequently present in subjects without recognized CHF. Furthermore, diastolic dysfunction as rigorously defined by comprehensive Doppler techniques is common, often not accompanied by recognized CHF and associated with marked increases in all-cause mortality.

REFERENCES

1. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography in the clinician's Rosetta stone. *J Am Coll Cardiol*. 1997;30:8-18.
2. Zile MR, Gaasch WH, Carroll JD, et al. Heart failure with normal ejection fraction: Is measurement of diastolic function necessary to make the diagnosis of diastolic heart failure. *Circulation*. 2001;104:779-782.
3. McDonagh TA, Morrison C, Lawrence A, et al. Symptomatic and asymptomatic left-ventricular systolic dysfunction in an urban population. *Lancet*. 1997; 35:829-833.
4. Mosterd A, Hoes AW, de Bruyne MC, et al. Prevalence of heart failure and left ventricular dysfunction in the general population: The Rotterdam Study. *Eur Heart J*. 1999;20:447-455.
5. Davies M, Hobbs F, Davis R, et al. Prevalence of left-ventricular systolic dysfunction and heart failure in the Echocardiographic Heart of England Screening study: a population based study. *Lancet*. 2001;358: 439-444.
6. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol*. 2001;38:2101-2113.
7. Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. *J Am Coll Cardiol*. 2001;37:1042-1048.
8. Bella JN, Palmieri V, Roman MJ, et al. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults: the Strong Heart Study. *Circulation*. 2002;105:1928-1933.
9. Senni M, Tribouilloy CM, Rodeheffer RJ, et al. Congestive heart failure in the community: a study of all incident cases in Olmsted County, Minnesota, in 1991. *Circulation*. 1998;98:2282-2289.
10. Melton LJ III. History of the Rochester Epidemiology Project. *Mayo Clin Proc*. 1996;71:266-274.
11. Redfield MM, Rodeheffer RJ, Jacobsen SJ, Mahoney DW, Bailey KR, Burnett JC Jr. Plasma brain natriuretic peptide concentration: impact of age and sex. *J Am Coll Cardiol*. 2002;40:976-982.
12. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure [published correction appears in *Arch Intern Med*. 1998;158:573]. *Arch Intern Med*. 1997;157:2413-2446.
13. Gillum RF, Fortmann SP, Prineas RJ, Kottke TE. International diagnostic criteria for acute myocardial infarction and acute stroke. *Am Heart J*. 1984;108: 150-158.
14. Quinones MA, Waggoner AD, Reduto LA, et al. A new, simplified and accurate method for determining ejection fraction with two-dimensional echocardiography. *Circulation*. 1981;64:744-753.
15. Starling MR, Crawford MH, Sorensen SG, Levi B, Richards KL, O'Rourke RA. Comparative accuracy of apical biplane cross-sectional echocardiography and gated equilibrium radionuclide angiography for estimating left ventricular size and performance. *Circulation*. 1981;63:1075-1084.
16. Jensen-Urstad K, Bouvier F, Hojer J, et al. Comparison of different echocardiographic methods with radionuclide imaging for measuring left ventricular ejection fraction during acute myocardial infarction treated by thrombolytic therapy. *Am J Cardiol*. 1998;81:538-544.
17. Michels VV, Moll PP, Miller FA, et al. The frequency of familial dilated cardiomyopathy in a series of patients with idiopathic dilated cardiomyopathy. *N Engl J Med*. 1992;326:77-82.
18. Ommen SR, Nishimura RA, Appleton CP, et al. The clinical utility of Doppler echocardiography and tissue Doppler imaging in estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. *Circulation*. 2000;102: 1788-1794.
19. Murray JA, Kennedy JW, Figley MM. Quantitative angiocardiography, II: the normal left atrial volume in man. *Circulation*. 1968;37:800-804.
20. Shub C, Klein AL, Zachariah PK, Bailey KR, Tajik AJ. Determination of left ventricular mass by echocardiography in a normal population: effect of age and sex in addition to body size. *Mayo Clin Proc*. 1994; 69:205-211.
21. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika*. 1994;81:515-526.
22. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. Congestive heart failure in subjects with normal vs reduced left ventricular ejection fraction. *J Am Coll Cardiol*. 1999;33:1948-1955.
23. Kitzman DW, Gardin JM, Gottdiener JS, et al. for the CHS Research Group. Cardiovascular Health Study. Importance of heart failure with preserved systolic function in patients > or =65 years of age. *Am J Cardiol*. 2001;87:413-419.
24. Devereux RB, Roman MJ, Liu JE, et al. Congestive heart failure despite normal left ventricular systolic function in a population-based sample: the Strong Heart Study. *Am J Cardiol*. 2000;86:1090-1096.
25. Gandhi SK, Powers JC, Nomeir AM, et al. The pathogenesis of acute pulmonary edema associated with hypertension. *Physiol Rev*. 2000;344:17-22.
26. Klein AL, Burstow DJ, Tajik AJ, Zachariah PK, Bailey KR. Effects of age on left ventricular dimensions and filling dynamics in 117 normal persons. *Mayo Clin Proc*. 1994;69:212-214.
27. Lakatta EG. Cardiovascular regulatory mechanisms in advanced age. *Physiol Rev*. 1993;73:413-467.
28. Sobue T, Yokota M, Iwase M, Ishihara H. Influence of left ventricular hypertrophy on left ventricular function during dynamic exercise in the presence or absence of coronary artery disease. *J Am Coll Cardiol*. 1995;25:91-98.
29. Hart CY, Meyer MD, Tazelaar HD, Grande JP, et al. Load vs humoral activation in the genesis of early hypertensive heart disease. *Circulation*. 2001;104: 215-220.
30. Yamamoto K, Nishimura RA, Chaliki HP, Appleton CP, Holmes DR Jr, Redfield MM. Determination of left ventricular filling pressure by Doppler echocardiography in patients with coronary artery diseases: the critical role of left ventricular systolic function. *J Am Coll Cardiol*. 1997;30:1819-1826.
31. Devereux RB, Roman MJ, Paranicas M, et al. A population-based assessment of left ventricular systolic dysfunction in middle-aged and older adults: the Strong Heart Study. *Am Heart J*. 2001;141: 439-446.
32. Gottdiener JS, McClelland RL, Marshall R, et al. Outcome of congestive heart failure in elderly persons: influence of left ventricular systolic function: the Cardiovascular Health Study. *Ann Intern Med*. 2002; 137:631-639.
33. Lloyd-Jones DM. The risk of congestive heart failure: sobering lessons from the Framingham Heart Study. *Curr Cardiol Rep*. 2001;3:184-190.
34. Yamamoto K, Burnett JC Jr, Jougasaki M, et al. Superiority of brain natriuretic peptide as a hormonal marker of ventricular systolic and diastolic dysfunction and ventriuclar hypertrophy. *Hypertension*. 1996; 28:988-994.
35. Yamamoto K, Burnett JC Jr, Bermudez EA, Jougasaki M, Bailey KR, Redfield MM. Clinical criteria and biochemical markers of systolic dysfunction. *J Card Fail*. 2000;6:194-200.
36. Maisel AS, Koon J, Krishnaswamy P, et al. Utility of B-natriuretic peptide as a rapid, point-of-care test for screening patients undergoing echocardiography to determine left ventricular dysfunction. *Am Heart J*. 2001; 141:367-374.
37. McDonagh TA, Robb SD, Murdoch DR, et al. Biochemical detection of left-ventricular systolic dysfunction. *Lancet*. 1998;351:9-13.
38. Lubien E, DeMaria A, Krishnaswamy P, et al. Utility of B-natriuretic peptide in detecting diastolic dysfunction: comparison with Doppler velocity recordings. *Circulation*. 2002;105:595-601.
39. Vasan RS, Benjamin EJ, Larson MG, et al. Plasma natriuretic peptides for community screening for left ventricular hypertrophy and systolic dysfunction: the Framingham heart study. *JAMA*. 2002;288:1252-1259.
40. Hurrell DG, Nishimura RA, Ilstrup DM, Appleton CP. Utility of preload alteration in assessment of left ventricular filling pressure by Doppler echocardiography: a simultaneous catheterization and Doppler echocardiographic study. *J Am Coll Cardiol*. 1997; 30:459-467.