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Outcome of Congestive Heart Failure in Elderly Persons: Influence of Left Ventricular Systolic Function

The Cardiovascular Health Study

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Background: Most persons with congestive heart failure are elderly, and many elderly persons with congestive heart failure have normal left ventricular systolic function.

Objective: To evaluate the relationship between left ventricular systolic function and outcome of congestive heart failure in elderly persons.

Design: Population-based longitudinal study of coronary heart disease and stroke.

Setting: Four U.S. sites: Forsyth County, North Carolina; Sacramento County, California; Allegheny County, Pennsylvania; and Washington County, Maryland.

Participants: 5888 persons who were at least 65 years of age and were recruited from the community.

Measurements: Total mortality and cardiovascular morbidity and mortality.

Results: Of 5532 participants, 269 (4.9%) had congestive heart failure. Among these, left ventricular function was normal in 63%, borderline decreased in 15%, and overtly impaired in 22%. The mortality rate was 25 deaths per 1000 person-years in the reference group (no congestive heart failure and normal left ventricular function at baseline); 154 deaths per 1000 person-years in participants with congestive heart failure and impaired left ventricular systolic function; 87 and 115 deaths per 1000 person-years in participants with congestive heart failure and normal or borderline systolic function, respectively; and 89 deaths per 1000 person-years in persons with impaired left ventricular function but no congestive heart failure. Although the risk for death from congestive heart failure was lower in persons with normal systolic function than in those with impaired function, more deaths were associated with normal systolic function because more persons with heart failure fall into this category.

Conclusions: Community-dwelling elderly persons, especially those with impaired left ventricular function, have a substantial risk for death from congestive heart failure. However, more deaths occur from heart failure in persons with normal systolic function because left ventricular function is more often normal than impaired in elderly persons with heart failure.

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Congestive heart failure is the most frequent cause of hospitalization in persons 65 years of age or older, accounting for more than 875 000 admissions each year in the United States (1). Moreover, aging of the population, increased susceptibility of elderly hypertensive persons to congestive heart failure (2), decreasing incidence of and death from stroke, and improved survival after acute myocardial infarction have increased the number of patients at risk for congestive heart failure (1, 3, 4).

The clinical syndrome of congestive heart failure occurs over a broad range of underlying left ventricular systolic function (5–7). Compared with persons younger than 65 years of age, more elderly persons with congestive heart failure have normal systolic function (5, 8). Elevated pulmonary venous pressure, which accounts at least in part for the clinical manifestations of congestive heart failure, is likely to result from impaired diastolic ventricular filling (9). This impairment may be the consequence of diminished systolic function or of other causes (10–14) that may result in decreased myocardial compliance in the absence of systolic dysfunction.

The probability of survival diminishes substantially after congestive heart failure is diagnosed (15, 16). However, studies have differed about the impact of left ventricular systolic function on survival (17–23). We tested the hypothesis that congestive heart failure confers increased morbidity and mortality in elderly persons even in the presence of normal or only mildly impaired left ventricular systolic function. We also hypothesized that impaired systolic function would be independently associated with greater risk than normal or borderline function.

METHODS

Study Sample

The Cardiovascular Health Study, designed to assess cardiovascular disease, cardiovascular disease outcomes, and risk factors, identified adults from the Health Care Financing Administration Medicare enrollment lists in four widely separated U.S. communities, along with other household members who were older than 65 years of age at study enrollment. Recruitment centers were located in Washington County, Maryland; Forsyth County, North Carolina; Sacramento County, California; and Allegheny County, Pennsylvania. Persons were excluded from the Cardiovascular Health Study if they were receiving active treatment for cancer, were wheelchair-bound or institutionalized, or were unable to participate in the examination. Prevalent coronary artery disease, stroke, and heart failure were not exclusion criteria. When we included both

Context

Most patients with congestive heart failure (CHF) are 65 years of age or older.

Older patients more often have CHF with normal left ventricular systolic function than younger patients.

How left ventricular systolic function affects prognosis of CHF in older patients is not clear.

Contribution

In this population-based study of 5532 older adults, 4.9% had CHF with normal (63%), borderline decreased (15%), or impaired (22%) left ventricular systolic function.

Forty-five percent of those with CHF and 16% of those without CHF died within 6 to 7 years.

Among those with CHF, death rates were higher with decreased versus normal left ventricular systolic function.

–The Editors

the original cohort (recruited in 1989 to 1990) and those enrolled when the study was expanded to include more African-American persons (in 1992 to 1993), data were available from 5888 study participants. Details of the design, sampling, and recruitment of the Cardiovascular Health Study, as well as the interview and examination, have been published previously (24). Self-report of cardiovascular and pulmonary diseases was validated according to standardized criteria through assessment of medications, medical records, and relevant information obtained during the initial examination. Further evaluation involved fasting blood chemistry tests, measurement of blood pressure and heart rate, anthropometric measurements, electrocardiography, echocardiography, carotid ultrasonography, and other objective measurements. Participants without an interpretable echocardiogram and those with significant aortic or mitral stenosis, greater than moderate mitral regurgitation, or at least moderately severe aortic regurgitation were excluded from our study.

Adjudication of Congestive Heart Failure

Details of the methods used to assess the prevalence of congestive heart failure among participants in the Cardiovascular Health Study have been reported previously (25, 26). An expert panel adjudicated the index event of congestive heart failure by reviewing all pertinent data on the hospitalization or outpatient visit, including history, physical examination, report of chest radiography, and medication usage. Self-report of a physician diagnosis of congestive heart failure was confirmed by documentation in the medical record of a constellation of symptoms (shortness of breath, fatigue, orthopnea, paroxysmal nocturnal dyspnea) and physical signs (edema, pulmonary rales, gallop rhythm, displaced left ventricular apical impulse) or by supporting clinical findings, such as those on chest radiography. Diagnosis of congestive heart failure was also confirmed if, in addition to having a previous physician diagnosis, the participant was receiving medical therapy for congestive heart failure (a current prescription of a diuretic and digitalis or a vasodilator [nitroglycerin, hydralazine, or angiotensin-converting enzyme inhibitor]).

Adjudication of Outcome Events

Throughout the follow-up period, participants were interviewed every 6 months and follow-up examinations

Table 1. **Baseline Characteristics of Participants by Study Group***

Characteristic	No CHF, Normal LV Systolic Function (n = 4864)	No CHF, Borderline LV Systolic Function (n = 263)	No CHF, Impaired LV Systolic Function (n = 136)
Age, *y*	72.7 ± 5.5	73.9 ± 6.1	74.5 ± 5.7
Men, *n (%)*	1940 (39.9)	170 (64.6)	101 (74.3)
African-American ethnicity, *n (%)*	613 (12.6)	30 (11.4)	15 (11.0)
Weight, *kg*	72.1 ± 14.3	77.2 ± 14.3	77.0 ± 14.2
Systolic blood pressure, *mm Hg*	135.9 ± 21.3	136.0 ± 20.4	138.2 ± 23.3
Diastolic blood pressure, *mm Hg*	70.7 ± 11.1	70.4 ± 12.6	72.5 ± 12.5
Hypertension, *n (%)*	2195 (45.1)	148 (56.3)	63 (46.3)
Diabetes, *n (%)*	518 (10.7)	48 (18.3)	21 (15.4)
Coronary heart disease, *n (%)*	725 (14.9)	92 (35.0)	79 (58.1)
Serum creatinine concentration, *μmol/L (mg/dL)*	91 ± 27 (1.03 ± 0.3)	106 ± 53 (1.20 ± 0.6)	108 ± 35 (1.22 ± 0.4)
Serum cholesterol level, *mmol/L (mg/dL)*	5.5 ± 1.0 (212.6 ± 38.7)	5.4 ± 1.0 (207.0 ± 40.1)	5.2 ± 1.0 (202.9 ± 41.6)
FEV_1, *L/min*	2.07 ± 0.7	2.14 ± 0.7	2.14 ± 0.7
Ankle–arm index < 0.9, *n (%)*	535 (11.0)	42 (16.0)	38 (27.9)
Alcohol intake, *drinks/wk*	2.51 ± 6.3	3.26 ± 7.7	1.92 ± 5.3
Internal carotid intima–media thickness, *mm*	1.41 ± 0.6	1.58 ± 0.6	1.74 ± 0.6
Common carotid intima–media thickness, *mm*	1.05 ± 0.2	1.11 ± 0.3	1.16 ± 0.2
Atrial fibrillation on electrocardiography, *n (%)*	86 (1.8)	13 (4.9)	9 (6.6)
Early mitral inflow velocity on Doppler ultrasonography, *cm/s*	71 ± 17	69 ± 20	65 ± 19
Late mitral inflow velocity on Doppler ultrasonography, *cm/s*	80 ± 22	80 ± 25	76 ± 28
Ratio of early to late mitral inflow velocity	1.25 ± 5.0	0.98 ± 0.8	1.42 ± 3.0
LV mass on electrocardiography, *g*	150.3 ± 29.5	171.4 ± 38.1	185.3 ± 40.7
Mitral regurgitation, *n (%)*	329 (6.8)	24 (9.1)	19 (14.0)

* Values presented with plus/minus sign are the mean ± SD. Differences in all variables among the six groups (except late mitral inflow velocity) were statistically significant for unadjusted analyses and for analyses adjusted for age and sex ($P < 0.01$). CHF = congestive heart failure; LV = left ventricular.

were conducted annually at each local center. Outcome events were tabulated on the basis of report of physician-diagnosed myocardial infarction or stroke and were then confirmed as described earlier. Deaths were confirmed by review of medical records and death certificates, as well as review of data on hospitalizations from the Health Care Financing Administration Medicare database on health care utilization. Cardiovascular death was classified according to criteria published previously (27). Briefly, myocardial infarction, stroke, sudden cardiac death, aortic aneurysm, peripheral vascular disease, mesenteric events, and congestive heart failure were included as immediate causes of death. Through these methods, as well as through interviews of contacts and proxies for participants lost to follow-up, we accounted for vital status in 100% of our participants.

Echocardiography and Left Ventricular Systolic Function

The design for echocardiographic study of participants in the Cardiovascular Health Study has been published previously (28). Briefly, two-dimensional echocardiography was performed at the baseline visit for the original cohort and at 2 years after the baseline visit for the second cohort. All echocardiograms were interpreted at a centralized core echocardiography laboratory by persons blinded to participants' clinical information. To avoid lost statistical power due to an inability to determine left ventricular mass on echocardiography in a substantial number of participants, left ventricular mass was estimated by electrocardiography using methods published elsewhere (29). Valvular regurgitation and stenosis were assessed as previously described (28). Global left ventricular systolic function was qualitatively assessed on two-dimensional echocardiography as normal, borderline, or impaired, corresponding to an ejection fraction of 0.55 or greater, 0.45 to 0.54, and less than 0.45, respectively. Qualitative systolic function was assessable in 5649 (96%) of the original and second Cardiovascular Heath Study cohorts. The interreader agreement was 95% ($\kappa = 0.32$) based on quality-control rereads of 370 study echocardiograms, and the intrareader agreement was 99% in 158 rereads ($\kappa = 0.92$) (30).

Clinical Assessment and Measurements

At study enrollment, clinically evident coronary artery disease was determined as described previously (24–26). Diabetes mellitus was defined according to history reported on the questionnaire and current use of insulin or oral hypoglycemic medication. The ankle–arm index (the ratio of supine systolic blood pressure at the ankle to that at the brachial artery, a measure of lower-extremity arterial occlusive disease [31]) was measured at baseline in both the original and second cohort. Baseline analyses of fasting serum chemistry values and fasting lipid measurements were also performed for both cohorts. Measures of pulmonary function, performed at the baseline visit for the original cohort and at 1 year after the baseline visit for the second cohort, included FVC and FEV_1. At the baseline visit for both cohorts, common and internal intima–media thickness of the carotid artery was measured. Digitally recorded twelve-lead electrocardiograms, obtained at the baseline examination for both cohorts, were analyzed as described elsewhere (25, 26).

Study Groups

To evaluate the relationship between left ventricular systolic function and outcome of congestive heart failure,

Table 1—Continued

CHF, Normal LV Systolic Function ($n = 170$)	CHF, Borderline LV Systolic Function ($n = 39$)	CHF, Impaired LV Systolic Function ($n = 60$)
74.8 ± 6.0	73.2 ± 6.0	74.0 ± 5.5
75 (44.1)	19 (48.7)	38 (63.3)
32 (18.8)	10 (25.6)	14 (23.3)
75.5 ± 17.7	77.0 ± 17.4	74.6 ± 14.5
137.9 ± 26.8	136.3 ± 20.6	126.6 ± 22.0
67.8 ± 13.4	67.7 ± 12.2	66.1 ± 12.3
101 (59.4)	28 (71.8)	34 (56.7)
45 (26.5)	14 (35.9)	14 (23.3)
98 (57.6)	27 (69.2)	47 (78.3)
106 ± 44 (1.20 ± 0.5)	103 ± 27 (1.16 ± 0.3)	137 ± 8 (1.55 ± 1.1)
5.0 ± 0.9 (197.1 ± 38.2)	5.2 ± 1.1 (202.9 ± 43.3)	5.1 ± 1.1 (200.3 ± 44.1)
1.75 ± 0.6	1.77 ± 0.5	1.96 ± 0.6
39 (22.9)	10 (25.6)	18 (30.0)
1.50 ± 5.0	2.11 ± 6.8	0.76 ± 3.1
1.64 ± 0.6	1.70 ± 0.7	1.80 ± 0.7
1.11 ± 0.2	1.11 ± 0.2	1.14 ± 0.3
25 (14.7)	5 (12.8)	3 (5.0)
78 ± 27	83 ± 30	77 ± 34
77 ± 33	84 ± 33	82 ± 34
2.62 ± 8.6	2.55 ± 6.3	1.91 ± 4.9
162.6 ± 36.7	175.2 ± 32.0	219.5 ± 77.3
16 (9.4)	9 (23.1)	15 (25.0)

Table 2. **Medication Use by Study Group***

Group (Participants)†	β-Blockers‡	ACE Inhibitors§	Lipid-Lowering Drugs‖	Diuretics§	Calcium-Channel Blockers§	Frequent Aspirin Use§¶	Digitalis§
	←			*n* (%)			→
Study subgroups							
No CHF, normal LV systolic function (*n* = 4862)	607 (12.5)	303 (6.2)	263 (5.4)	1282 (26.4)	574 (11.8)	1138 (23.4)	283 (5.8)
No CHF, borderline LV systolic function (*n* = 261)	46 (17.6)	27 (10.3)	14 (5.4)	79 (30.3)	50 (19.2)	71 (27.2)	26 (10.0)
No CHF, impaired LV systolic function (*n* = 136)	20 (14.7)	12 (8.8)	11 (8.1)	42 (30.9)	30 (22.1)	43 (31.6)	26 (19.1)
CHF, normal LV systolic function (*n* = 170)	29 (17.1)	42 (24.7)	8 (4.7)	100 (58.8)	52 (30.6)	63 (37.1)	70 (41.2)
CHF, borderline LV systolic function (*n* = 39)	3 (7.7)	11 (28.2)	1 (2.6)	29 (74.4)	18 (46.2)	18 (46.2)	18 (46.2)
CHF, impaired LV systolic function (*n* = 60)	4 (6.7)	25 (41.7)	1 (1.7)	47 (78.3)	18 (30.0)	25 (41.7)	31 (51.7)
Alternate subgroups							
No CHF (*n* = 5259)	673 (12.8)	342 (6.5)	288 (5.5)	1403 (26.7)	654 (12.4)	1252 (23.8)	335 (6.4)
CHF (*n* = 269)	36 (13.4)	78 (29.0)	10 (3.7)	176 (65.4)	88 (32.7)	106 (39.4)	119 (44.2)
Normal LV systolic function (*n* = 5032)	636 (12.6)	345 (6.9)	271 (5.4)	1382 (27.5)	626 (12.4)	1201 (23.9)	353 (7.0)
Borderline LV systolic function (*n* = 300)	49 (16.3)	38 (12.7)	15 (5.0)	108 (36.0)	68 (22.7)	89 (29.7)	44 (14.7)
Abnormal LV systolic function (*n* = 196)	24 (12.2)	37 (18.9)	12 (6.1)	89 (45.4)	48 (24.5)	68 (34.7)	57 (29.1)

* ACE = angiotensin-converting enzyme; CHF = congestive heart failure; LV = left ventricular.
† For 115 participants, values for medications were missing. Participants with significant valvular heart disease and missing or invalid results on echocardiography were excluded.
‡ $P = 0.035$ for comparisons among study subgroups.
§ $P = 0.001$ for comparisons among study subgroups.
‖ $P > 0.2$ for comparisons among study subgroups.
¶ Frequent aspirin use was defined as a prescription for aspirin or >7 days of use in the previous 2 weeks.

six groups were identified by congestive heart failure status and left ventricular systolic function at baseline: 1) no congestive heart failure and normal left ventricular systolic function, 2) no congestive heart failure and borderline systolic function, 3) no congestive heart failure and impaired systolic function, 4) congestive heart failure and normal systolic function, 5) congestive heart failure and borderline systolic function, and 6) congestive heart failure and impaired systolic function.

Statistical Analysis

Chi-square tests or analysis of variance was used for unadjusted analyses of the associations among groups and baseline variables. Age- and sex-adjusted associations were investigated by using logistic regression models or analysis of covariance, using the six subgroups as predictors (32).

Event rates per 1000 person-years at risk are presented for each type of incident event. Cox proportional hazard regression techniques were used to examine the association of the six subgroups with time to incident events after adjustment for covariates (33). Covariates included factors previously associated with poor outcome in other population-based investigations of survival, as well as baseline variables significantly associated with incident events in our study. These included age, sex, black ethnicity, weight, systolic blood pressure, diastolic blood pressure, diabetes, history of coronary heart disease, FEV_1, ankle–arm index dichotomized at 0.9, atrial fibrillation on electrocardiography, intima–media thickness for common and internal carotids, creatinine concentration, cholesterol level, alcoholic drinks per week, left ventricular mass, early and late mitral inflow velocity on Doppler ultrasonography, left atrial dimension, mitral regurgitation, medications (β-blockers, angiotensin-converting enzyme inhibitors, lipid-lowering drugs, diuretics, calcium-channel blockers, aspirin, digitalis), and clinic. In addition, we included a term to adjust for clustering within clinic, using the cluster(clinic) option of the coxph function in S-Plus 2000 (Insightful Corp., Seattle, Washington).

The variables for mitral regurgitation, cholesterol level, and lipid-lowering medications were highly nonsignificant and did not behave as confounders for group in any of the models. That is, once these variables were removed from the model, estimates of hazard ratios for levels of the group variable changed at most in the second decimal place. In addition, removal of these variables improved the results of the overall tests of the proportional hazards assumption so that all models satisfied a *P* value greater than or equal to 0.08. For these reasons, mitral regurgitation, cholesterol level, and lipid-lowering medications were omitted from all adjusted models.

A statistic (mortality impact, also known as population attributable risk) was calculated to express the impact of the clinical condition (congestive heart failure with normal, borderline, or impaired systolic function) on the expected population mortality rate, based on the mortality risk and the prevalence of the condition in our population-based

cohort (32). All statistical analyses were conducted by using S-Plus 2000, release 3.

Role of the Funding Source

This study was funded through contracts with the National Heart, Lung, and Blood Institute (NHLBI) and included substantial NHLBI involvement in data collection, analysis, and interpretation and manuscript preparation.

RESULTS

Prevalence of Congestive Heart Failure and Left Ventricular Function

Congestive heart failure was identified in 300 of 5888 participants (5.1%), and left ventricular systolic function was assessable in 5649 participants (96%). Of the 5532 participants remaining after those with significant valvular heart disease were excluded, 269 (4.9%) had congestive heart failure; 52% of these were women. Baseline left ventricular function was normal in 170 participants with congestive heart failure (63%), borderline in 39 (15%), and impaired in 60 (22%).

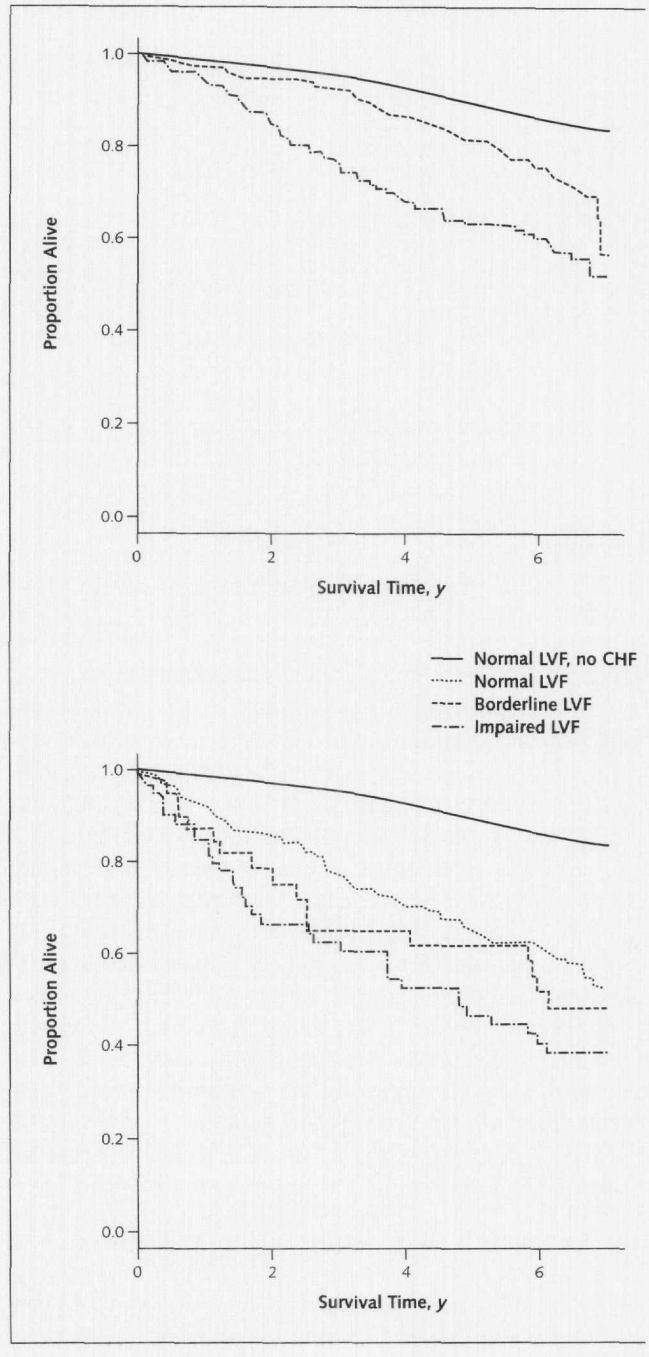
Baseline Characteristics of Study Groups

Comparison of baseline characteristics among groups is shown in **Table 1**. Compared with the other groups, the group with congestive heart failure and impaired left ventricular systolic function had lower mean systolic blood pressure, included more participants with clinically evident coronary artery disease and subclinical atherosclerosis (increased intima–media thickness of the internal carotid artery, low ankle–arm index), had higher serum creatinine concentrations, and had greater left ventricular mass. When we compared participants who had congestive heart failure and normal left ventricular function with those who had impaired function, the former group was older, had higher mean systolic blood pressure, included more women, included fewer persons with clinically evident coronary artery disease, had lower serum creatinine concentrations, and had lower left ventricular mass. Use of cardiovascular medications at baseline is shown in **Table 2**. Statistically significant differences were seen among study groups for all cardiac medications, with the exception of lipid-lowering drugs.

Unadjusted All-Cause Mortality

The mortality rate was 25 deaths per 1000 person-years in the reference group (no congestive heart failure and normal left ventricular function at baseline); 154 deaths per 1000 person-years in participants with congestive heart failure and impaired left ventricular systolic function; 87 and 115 deaths per 1000 person-years in participants with congestive heart failure and normal or borderline systolic function, respectively; and 89 deaths per 1000 person-years in persons with impaired left ventricular function but no congestive heart failure. Participants without congestive heart failure had a higher mortality rate with impaired ($P < 0.001$) and borderline ($P < 0.001$) left ventricular systolic function when compared with the reference group (no congestive heart failure and normal systolic function) (**Figure**).

Figure. **Unadjusted Kaplan–Meier survival curves for participants with no congestive heart failure (*CHF*) (*top*) and for those with CHF (*bottom*) based on left ventricular function (*LVF*).**



In participants with congestive heart failure, the all-cause mortality rate was 45% at a median follow-up of 6.4 years compared with 16% in those without congestive heart failure ($P < 0.001$). Participants with congestive heart failure and normal left ventricular function had a

Table 3. **Event Rates and Hazard Ratios***

Study Group	Nonfatal Myocardial Infarction			Stroke		
	Event Rate	Unadjusted Hazard Ratio in 383 Participants	Adjusted Hazard Ratio in 331 Participants	Event Rate	Unadjusted Hazard Ratio in 424 Participants	Adjusted Hazard Ratio in 340 Participants
No CHF, normal LV systolic function	10.9	1.0	1.0	12.5	1.0	1.0
No CHF, borderline LV systolic function	29.7	2.74 (2.0–3.8)	2.00 (1.4–2.8)	21.4	1.73 (1.2–2.5)	1.26 (0.9–1.7)
No CHF, impaired LV systolic function	36.8	3.39 (2.2–5.2)	1.42 (0.9–2.2)	33.0	2.67 (1.7–4.2)	1.27 (1.0–1.6)
CHF, normal LV systolic function	23.3	2.16 (1.3–3.5)	1.44 (0.6–3.4)	27.5	2.23 (1.4–3.5)	1.27 (0.9–1.8)
CHF, borderline LV systolic function	37.7	3.52 (1.5–8.5)	2.17 (1.2–4.0)	50.7	4.15 (2.0–8.8)	2.41 (1.3–4.5)
CHF, impaired LV systolic function	19.4	1.81 (0.7–4.9)	0.92 (0.4–2.1)	45.2	3.69 (1.9–7.2)	1.91 (1.3–2.7)

* Values in parentheses are 95% CIs. All hazard ratios are based on Cox proportional hazards models. Event rates are expressed as rates per 1000 person-years at risk. Adjusted models include the following terms: age, sex, African-American ethnicity, weight, systolic blood pressure, diastolic blood pressure, diabetes, history of coronary heart disease, FEV_1, ankle–arm index dichotomized at 0.9, atrial fibrillation on electrocardiography, intima–media thickness for common and internal carotids, creatinine concentration, alcoholic drinks per week, LV mass, early and late mitral inflow velocity on Doppler ultrasonography, left atrial dimension, β-blockers, angiotensin-converting enzyme inhibitors, diuretics, calcium-channel blockers, digitalis, frequent aspirin use, clinic site, and a term to adjust for clustering within clinic. CHF = congestive heart failure; LV = left ventricular.

mortality rate that was significantly higher than that in the reference group ($P < 0.001$) (**Figure**) and was similar to that in participants with impaired function but no congestive heart failure. Impaired (but not borderline) left ventricular function was associated with higher mortality rates among participants with congestive heart failure ($P = 0.007$).

Adjusted All-Cause and Cardiovascular Mortality

After adjustment for covariates, the risk for all-cause mortality was significantly increased in persons with congestive heart failure and normal, borderline, or impaired left ventricular systolic function compared with the reference group (**Table 3**). The risk for all-cause mortality was also greater in participants with no congestive heart failure who had impaired or borderline left ventricular function.

The adjusted risk for cardiovascular mortality was increased in persons with borderline or impaired left ventricular function but no congestive heart failure and in persons with congestive heart failure and impaired left ventricular function. The risk was not significantly increased in persons with congestive heart failure and borderline left ventricular function (adjusted hazard ratio, 2.39 [95% CI, 0.9 to 6.1]) or congestive heart failure and normal left ventricular function (adjusted hazard ratio, 1.29 [CI, 0.9 to 1.9]).

Risk for Nonfatal Myocardial Infarction and Stroke

Compared with the reference group, all groups except the group with congestive heart failure and impaired left ventricular function were at increased risk for nonfatal myocardial infarction and stroke (**Table 3**). Participants with borderline left ventricular function with or without heart failure remained at risk for nonfatal myocardial infarction after adjustment for covariates, whereas participants in the other groups did not. Risk for stroke remained increased only in persons with congestive heart failure and borderline or impaired left ventricular function and was of borderline significance in those with impaired function but no heart failure.

Mortality Impact of Heart Failure with Normal versus Impaired Systolic Function

The mortality impact (population attributable risk) from any cause was greatest (7.5%) in the group with congestive heart failure and normal left ventricular function, reflecting the combined effect of moderate risk and high prevalence of heart failure in the presence of normal systolic function. In contrast, the mortality impact of congestive heart failure in participants with impaired systolic function was 5.9% despite the higher hazard ratio. This finding was due to the lower prevalence of impaired systolic function in persons with heart failure.

Discussion

Previous reports from the Cardiovascular Health Study have demonstrated that most community-based elderly persons with congestive heart failure have normal left ventricular systolic function (34); that normal systolic function most commonly precedes incident congestive heart failure (35); and that the predictors of congestive heart failure in elderly persons (35, 36) with or without systolic dysfunction include clinical and subclinical coronary heart disease, systolic blood pressure, inflammation, left atrial size, and diastolic dysfunction. Our principal finding is that community-based elderly persons with congestive heart failure have a substantial risk for death, even in the presence of normal or borderline decreased left ventricular systolic function. Although the adjusted mortality risk was greatest in participants with congestive heart failure and abnormal left ventricular systolic function, only a minority of community-based elderly persons were in this category. Therefore, the mortality impact of death from any cause after a diagnosis of congestive heart failure was greater in persons with normal left ventricular systolic function than in those with borderline or impaired function. Since we excluded participants with clinically significant valvular heart disease, our findings probably represent the adverse outcome of what has commonly been termed

Table 3—**Continued**

Cardiovascular Mortality			All-Cause Mortality		
Event Rate	Unadjusted Hazard Ratio in 397 Participants	Adjusted Hazard Ratio in 317 Participants	Event Rate	Unadjusted Hazard Ratio in 952 Participants	Adjusted Hazard Ratio in 759 Participants
9.0	1.0	1.0	25.1	1.0	1.0
33.3	3.71 (2.7–5.0)	2.08 (1.7–2.6)	51.0	2.05 (1.6–2.6)	1.25 (1.1–1.4)
50.5	5.80 (4.0–8.3)	2.13 (1.7–2.7)	88.7	3.69 (2.8–4.8)	1.83 (1.2–2.7)
40.9	4.72 (3.3–6.8)	1.29 (0.9–1.9)	87.0	3.62 (2.8–4.6)	1.48 (1.2–1.8)
67.9	8.03 (4.3–15.1)	2.39 (0.9–6.1)	115.4	4.94 (3.1–8.0)	2.40 (1.2–4.6)
98.1	11.74 (7.5–18.3)	2.14 (1.5–3.1)	154.1	6.70 (4.7–9.5)	1.88 (1.0–3.4)

isolated diastolic heart failure (37). However, we recognize that without measures of diastolic function, this is a diagnosis of exclusion. Of particular interest in our study was the finding that the adjusted risk for all-cause and cardiovascular death was similar in participants with no clinical congestive heart failure but impaired systolic function and participants with congestive heart failure and impaired function, although the former group included more than twice as many persons as the latter. The 6-year mortality rate of 45% in participants reporting congestive heart failure was somewhat lower than the rate of 60% to 75% reported in other epidemiologic studies (1, 15, 22) but was highly statistically significant compared with persons without congestive heart failure, in whom the 6-year mortality rate was 16%.

Although left ventricular systolic performance has been established as an important predictor of outcome in persons with acute myocardial infarction (38, 39) and those with symptomatic ventricular arrhythmias (40, 41), studies differ about the impact of systolic function on prognosis after congestive heart failure is diagnosed (17, 22, 23, 39, 42–44). We extended previous findings (22, 23) by evaluating a community-based sample made up exclusively of elderly persons and determining that congestive heart failure in elderly persons is associated with poor prognosis with or without impaired left ventricular systolic function. In contrast to the findings of the Olmstead County study (22) and the recent study published by the Italian Network on Congestive Heart Failure Investigators (44), we found that impaired systolic function was associated with greater risk for death than normal systolic function after a diagnosis of congestive heart failure. Although data from previous studies are conflicting (1, 15), we also found that this association was independent of male sex. Another finding of our study, not previously underscored in the literature, was the observation that the mortality impact of congestive heart failure was greater in elderly persons with normal left ventricular systolic function than in those with impaired systolic function, reflecting the lower prevalence of impaired systolic function.

It is of interest that the relationship between borderline left ventricular function and increased risk for nonfatal myocardial infarction persisted in adjusted models. This suggests that a mild and clinically inapparent decrease in left ventricular function nonetheless indicates increased risk for myocardial infarction, even after other markers of atherosclerosis severity are taken into account.

The six groups in our study were based in part on a qualitative assessment of global left ventricular systolic function. However, this assessment was performed in a centralized, experienced core laboratory with multiple quality controls. The articulation and accurate application of an appropriate definition of the clinical syndrome of congestive heart failure have been problematic in clinical studies. Since this was an epidemiologic study, we cannot definitively exclude the possibility that some participants classified as having congestive heart failure may have had dyspnea from noncardiac causes. To minimize such a possibility, some previous studies have required the presence of substantial decreases in left ventricular systolic ejection fraction for diagnosis. However, as our findings suggest, this would create a tautology by which it would not be possible to identify congestive heart failure in the absence of systolic dysfunction. It has been shown that acute pulmonary edema can occur in the presence of normal systolic function (45, 46) and that left atrial pressure is increased at rest and during exercise in patients with congestive heart failure and normal systolic function, as occurs in affected patients with impaired systolic function (9). Also, since many persons in this and other studies (45) have decreased systolic function without congestive heart failure, the finding of decreased systolic function may not always be helpful in determining whether dyspnea or suspicious roentgenographic findings are of cardiac origin.

The term *diastolic heart failure* has been used to describe congestive heart failure with normal left ventricular systolic function in the absence of valvular disease caused by physiologic characteristics of heart failure. Criteria have recently been proposed for this entity (37), including determination of normal ventricular systolic function within

72 hours of the sentinel event of clinical heart failure (that is, "probable" diastolic heart failure) and invasive measurement of abnormal myocardial relaxation (that is, "definite" diastolic heart failure). Invasive measurement of myocardial relaxation was not possible in our epidemiologic study and may not be relevant to clinical practice. We did not use other scoring systems or criterion-based algorithms for diagnosis of congestive heart failure.

In our study, ventricular systolic function was determined at a baseline examination variably remote from the sentinel clinical event of congestive heart failure. It has been shown, however, that systolic function may remain relatively stable after the onset of clinical findings of heart failure (46). We found that more participants had congestive heart failure and normal left ventricular systolic function than has previously been reported (5). This may be due to survival effects, whereby persons with particularly poor systolic function would be more likely to die or be otherwise unavailable for evaluation. It is also possible that systolic function may have improved between the onset of congestive heart failure and the time of the study echocardiography, although previous reports suggest that this is uncommon (7, 46). Notably, tabulation of clinical echocardiography reports retrieved from 145 of 170 cases of incident congestive heart failure in the Cardiovascular Health Study showed that 57% of persons had normal left ventricular systolic function at the time of hospitalization for congestive heart failure (36). Also, the presumably better health of our noninstitutionalized sample compared with other study samples (22, 23) may have resulted in selection of more participants with congestive heart failure and normal systolic function.

Up to 88% of congestive heart failure cases (3, 22) and 90% of deaths from congestive heart failure (48) occur in elderly persons. Despite this, however, most epidemiologic studies of heart failure and treatment trials on which current principles of heart failure pharmacotherapy are based have addressed a predominantly male population younger than 65 years of age with substantially impaired left ventricular systolic function (49–54). Such studies generally require a ventricular ejection fraction of less than 0.45, or even less than 0.35, as a criterion for enrollment. Therefore, the results of such clinical trials may not be applicable to elderly persons and others with congestive heart failure and preserved left ventricular function.

Elderly persons have a substantial risk for death after a diagnosis of congestive heart failure, and normal left ventricular systolic function does not ensure favorable outcome. Given the large proportion of elderly persons in the population, the greatest opportunity for reducing death from heart failure may lie in the successful treatment of those with normal left ventricular systolic function.

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