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The Natural History of Left Ventricular Geometry in the Community

Clinical Correlates and Prognostic Significance of Change in LV Geometric Pattern

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ABSTRACT

OBJECTIVES This study sought to evaluate pattern and clinical correlates of change in left ventricular (LV) geometry over a 4-year period in the community; it also assessed whether the pattern of change in LV geometry over 4 years predicts incident cardiovascular disease (CVD), including myocardial infarction, heart failure, and cardiovascular death, during an additional subsequent follow-up period.

BACKGROUND It is unclear how LV geometric patterns change over time and whether changes in LV geometry have prognostic significance.

METHODS This study evaluated 4,492 observations (2,604 unique Framingham Heart Study participants attending consecutive examinations) to categorize LV geometry at baseline and after 4 years. Four groups were defined on the basis of the sex-specific distributions of left ventricular mass (LVM) and relative wall thickness (RWT) (normal: LVM and RWT <80th percentile; concentric remodeling: LVM <80th percentile but RWT ≥80th percentile; eccentric hypertrophy: LVM ≥80th percentile but RWT <80th percentile; and concentric hypertrophy: LVM and RWT ≥80th percentile).

RESULTS At baseline, 2,874 of 4,492 observations (64%) had normal LVM and RWT. Participants with normal geometry or concentric remodeling progressed infrequently (4% to 8%) to eccentric or concentric hypertrophy. Change from eccentric to concentric hypertrophy was uncommon (8%). Among participants with concentric hypertrophy, 19% developed eccentric hypertrophy within the 4-year period. Among participants with abnormal LV geometry at baseline, a significant proportion (29% to 53%) reverted to normal geometry within 4 years. Higher blood pressure, greater body mass index (BMI), advancing age, and male sex were key correlates of developing an abnormal geometry. Development of an abnormal LV geometric pattern over 4 years was associated with increased CVD risk (140 events) during a subsequent median follow-up of 12 years (adjusted-hazards ratio: 1.59; 95% confidence interval: 1.04 to 2.43).

CONCLUSIONS The longitudinal observations in the community suggest that dynamic changes in LV geometric pattern over time are common. Higher blood pressure and greater BMI are modifiable factors associated with the development of abnormal LV geometry, and such progression portends an adverse prognosis. (J Am Coll Cardiol Img 2014;7:870–8)

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The left ventricle (LV) remodels over the life course as an adaptive response to aging, exposure to cardiovascular disease (CVD) risk factors, and myocardial injury (1). Left ventricular mass (LVM) and relative wall thickness (RWT) (ratio of LV wall thickness and LV internal dimensions) are important echocardiographic measures of LV remodeling. Different LV geometric patterns can be distinguished on the basis of whether RWT and LVM are normal versus increased: normal geometry (LVM and RWT are normal), concentric remodeling (increased RWT but normal LVM), concentric hypertrophy (LVM *and* RWT are increased), and eccentric hypertrophy (increased LVM with normal RWT) (2). Both increased LVM (3,4) and abnormal LV geometry patterns (5) adversely affect prognosis and are associated with impaired cardiac systolic and diastolic dysfunction (6), as well as with increased risk of CVD events and all-cause mortality prospectively (5,7–10).

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Information is very limited regarding how LV geometric patterns change over time and the determinants of such change. Furthermore, it is unclear whether changes in LV geometric patterns antedate the development of CVD, including heart failure. In animal models, a temporal sequence of change in LV geometric patterns has been observed, with concentric hypertrophy leading to LV dilation and eventually to overt heart failure (11). However, epidemiological evidence for such sequential changes in LV geometric patterns in the community is scant. Specifically, it is unclear whether concentric hypertrophy changes to eccentric hypertrophy (which can result from significant LV dilation or from an increase in LVM without significant concentricity or LV dilation) (12,13).The correlates and prognosis associated with such changes in LV geometry are also unknown.

The authors hypothesized that exposure to multiple cardiovascular risk factors adversely influences the natural history of LV geometry. They also hypothesized that worsening of LV geometry is associated with increased risk of CVD.

METHODS

STUDY SAMPLE. The recruitment and phenotyping of the Framingham Offspring Study have been described elsewhere (14). At each quadrennial visit, participants undergo a targeted medical history and physical examination, standardized anthropometry, and laboratory measurement of CVD risk factors. Attendees at examination cycles 4, 5, and 6 were eligible for the present investigation if they attended consecutive examinations and had available echocardiograms. The authors excluded persons with prevalent myocardial infarction or heart failure at these examinations (n = 490). The study protocols were approved by the Boston University Medical Center Institutional Review Board. The study complies with the Declaration of Helsinki. Written informed consent has been obtained from the participants.

ECHOCARDIOGRAPHIC MEASUREMENTS. Echocardiograms were routinely obtained at Offspring examination cycles 4 (1987 to 1990), 5 (1991 to 1995), and 6 (1996 to 1998) as described previously and detailed in the Online Appendix (15). Four groups were defined on the basis of the sex-specific distributions of LVM and RWT: normal LV geometry (LVM and RWT <80th percentile), concentric remodeling (LVM <80th percentile but RWT ≥80th percentile), eccentric hypertrophy (LVM ≥80th percentile but RWT <80th percentile), and concentric hypertrophy (LVM and RWT ≥80th percentile). For each participant, the LV geometric pattern at baseline was compared with the pattern at the subsequent examination approximately 4 years later. To maximize statistical power, the authors pooled observations on the changes in LV geometry from examination cycle 4 to 5 and from cycle 5 to 6 (cross-sectional pooling, **Figure 1**). If a participant had echocardiograms done at examinations 4, 5, and 6, that person was included twice in the analyses: once describing the change from examination 4 to examination 5 (using examination 4 as the baseline) and the second describing the change from examination 5 to examination 6 (using examination 5 as the baseline). The authors used this pooling approach to increase precision of estimates and improve statistical power.

Left ventricular hypertrophy (LVH) and abnormal RWT were defined as values greater than the respective 80th sex-specific percentile at examination cycle 4 in those participants with available echocardiographic data (for men: LVM, 207 g and RWT, 0.419; for women: LVM, 170 g and RWT, 0.435). These reference values were also applied to examination cycles 5 and 6. In additional analyses, the authors used cut-points for LVH (LVM indexed to body surface area; ≤115 g/m^2 vs. >115 g/m^2 for men and ≤95 g/m^2 vs. >95 g/m^2 for women) and increased RWT (≤0.42 vs. >0.42) as published by the American Society of Echocardiography (ASE) (16). Because analyses on the basis of the ASE cut-points and those based on the 80th percentile cut-points yielded similar rates of transition, all analyses focused on the latter approach.

ABBREVIATIONS AND ACRONYMS

ASE = American Society of Echocardiography
BMI = body mass index
BP = blood pressure
CHD = coronary heart disease
CVD = cardiovascular disease
LV = left ventricular
LVEDD = left ventricular end-diastolic diameter
LVH = left ventricular hypertrophy
LVM = left ventricular mass
OR = odds ratio
RWT = relative wall thickness

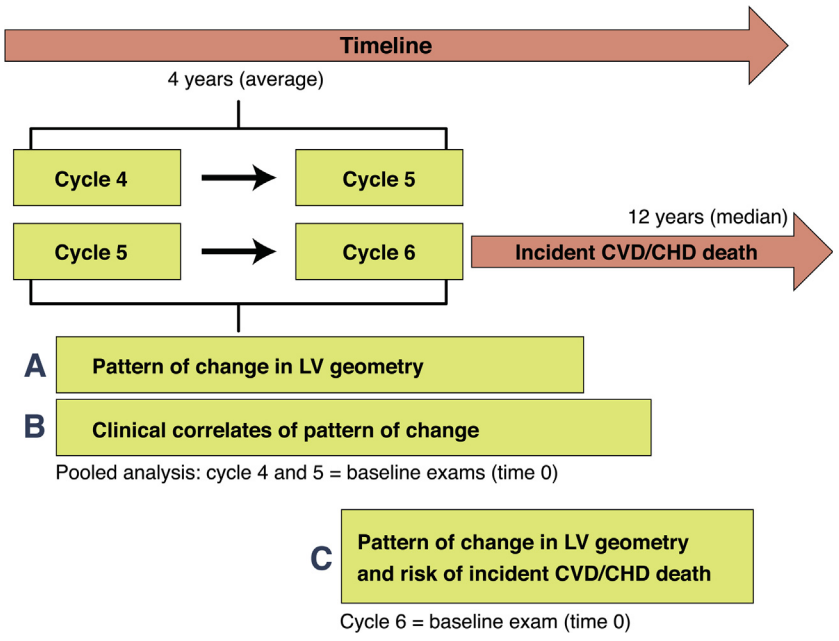

FIGURE 1 Study Design and Principal Analyses

CVD is defined as myocardial infarction, heart failure, or death from CHD. CHD = coronary heart disease; CVD = cardiovascular disease; LV = left ventricular.

ASSESSMENT OF CARDIOVASCULAR EVENTS. All participants are under surveillance for the development of CVD events including myocardial infarction, heart failure, and death from coronary heart disease (CHD). The diagnostic criteria for heart failure, myocardial infarction, and death from CHD have been described previously (17,18).

STATISTICAL METHODS. Differential missingness and survival bias according to baseline LV geometric pattern. During the 4-year period between consecutive examination cycles, approximately 1.3% (examination cycle 4→5) to 1.4% (examination cycle 5→6) of participants died; 6.5% (examination cycle 4→5) to 7.7% (examination cycle 5→6) did not attend the follow-up examination; and 16.6% (examination cycle 4→5) to 13.9% (examination cycle 5→6) of participants did attend the follow-up examination, but no echocardiographic data could be obtained. More details are provided in the Online Appendix.

Transition matrix. A transition matrix was constructed to cross-classify LV geometry at the baseline and subsequent examinations (cycles 4 to 5 and cycles 5 to 6, respectively, with cycles 4 and 5 serving as the baselines [time 0] for this analysis) to assess the proportion of participants who remained in the same category or developed a different geometric pattern at follow-up. Because rates of change in LV geometry were fairly similar from examination cycle 4 to 5 and from examination cycle 5 to 6, the authors pooled data across these consecutive examinations (Figure 1, label A).

Polytomous regression models. To evaluate clinical covariates associated with change in LV geometric patterns over time (Figure 1, label B), the authors used polytomous regression models to estimate odds ratios (ORs) and 95% confidence intervals for each abnormal geometric pattern (concentric remodeling, concentric hypertrophy, eccentric hypertrophy) on follow-up, with normal geometry at follow-up serving as a referent group. The authors focused on participants with a normal LV geometric pattern at baseline because most observations fell into this group. This study included sex, baseline age, systolic blood pressure (BP), body mass index (BMI), antihypertensive treatment, current smoking, diabetes, change in systolic BP and change in BMI (from baseline to follow-up), and the examination cycle as covariates. Furthermore, in those participants with an *abnormal* LV geometric pattern at baseline (concentric

remodeling, concentric hypertrophy, eccentric hypertrophy), the authors estimated ORs for the reversion to a normal LV geometric pattern on follow-up, with "remaining in the respective abnormal baseline category" serving as the referent category. These ORs were adjusted for the same set of covariates noted earlier.

Graphic display of changes in blood pressure, body mass index, left ventricular mass, and relative wall thickness. In participants with normal LV geometry at baseline, the authors displayed changes in LVM and RWT stratified by the LV geometric pattern on follow-up (Online Figure 1A). To elucidate the influence of BP and BMI, the change in these measures from baseline to follow-up was displayed graphically (Online Figure 1B).

Association of change in left ventricular geometry with cardiovascular disease (composite of incident myocardial infarction, heart failure, and death from CHD). The authors assessed whether change in LV geometry from examination cycle 5 to 6 was associated with incidence of CVD after examination cycle 6 (**Figure 1**, label C; examination cycle 6 serving as the baseline [time 0] for this analysis). For this purpose, participants were classified on the basis of how their LV geometry changed from cycle 5 to cycle 6 and 4 groups were defined:

1. Reference group: These participants with normal geometry or concentric remodeling at examination 5 remained in the same category.
2. Improvement of LV geometry: These participants reverted to normal geometry from any abnormal pattern at examination 5 or changed from eccentric or concentric hypertrophy to concentric remodeling.
3. Worsening of LV geometry: These participants developed an abnormal geometric pattern from a normal or concentric remodeling pattern. In addition, changes from eccentric to concentric LVH or vice versa were considered as worsening.
4. Remained high risk: Participants with concentric or eccentric hypertrophy who remained in the same category were considered as a separate category because these participants are at particularly high risk of CVD.

Cox proportional hazards regression models, adjusted for age and sex, were used to relate the change in LV geometry (independent categorical variable as defined earlier) to the incidence of CVD after examination cycle 6 (dependent variable), after confirming that the assumption of the proportionality of hazards was met. A composite endpoint was chosen because LV geometry has been previously related to all 3 components (myocardial infarction, heart failure, and death from CHD), and to maximize statistical power.

The authors performed sensitivity analyses defining LV geometric patterns on the basis of ASE cut-points. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina); a 2-tailed $p < 0.05$ was considered statistically significant.

RESULTS

The baseline characteristics of this sample (4,492 observations, 2,604 unique participants; mean age, 51 years; 59% women) by LV geometry pattern are shown in **Table 1**. The 2,604 participants (contributing 4,492 observations) represent 79% of the total number of participants who attended examination cycles 4, 5, and 6 ($n = 3,289$). Participants with eccentric and concentric hypertrophy were older and had higher BP and BMI compared with participants with normal LV geometry or concentric remodeling.

TRANSITION RATES OF LEFT VENTRICULAR GEOMETRIC PATTERN DURING A 4-YEAR FOLLOW-UP PERIOD. Most participants with *normal LV geometry at baseline* remained in that category (68%); approximately 20% progressed to concentric remodeling, but transition to eccentric or concentric hypertrophy was uncommon (**Table 2**, first row). More than one-half of the participants with *concentric remodeling at baseline* had normal LV geometry at follow-up, one-third remained in the concentric remodeling category, and only 6% to 7% progressed to eccentric and concentric hypertrophy (**Table 2**, second row). More than 40% of participants with *eccentric hypertrophy* at baseline had normal geometry at follow-up, whereas the development of concentric geometry was relatively uncommon (8%) (**Table 2**, third row). Approximately 19% of participants with concentric hypertrophy at baseline changed to eccentric hypertrophy, 29% reverted to normal LV geometry, and 17% reverted to concentric remodeling on follow-up (**Table 2**, last row). When ASE cut-points were used to define increased LVM and RWT, the proportion of participants changing from concentric hypertrophy to eccentric hypertrophy was lower (13%), but overall the transition matrix on the basis of ASE cut-points was not dissimilar (Online Table 1). The development of eccentric hypertrophy can result from an increase in left ventricular end-diastolic diameter (LVEDD) ("dilated LVH") (13), or it can be caused by an increase in LVM, but without either significant increase in LVEDD or increased concentricity ("indeterminate LVH") (12,13). To assess which subform of

TABLE 1 Baseline Characteristics of the Study Sample by Baseline LV Geometry

	Baseline LV Geometric Pattern			
	Normal Geometry (n = 2,874)	Concentric Remodeling (n = 820)	Eccentric Hypertrophy (n = 590)	Concentric Hypertrophy (n = 208)
Clinical features				
Women	59	61	62	34
Age, yrs	50 ± 10	54 ± 9	51 ± 10	58 ± 9
Systolic BP, mm Hg	121 ± 17	127 ± 18	128 ± 19	137 ± 20
Diastolic BP, mm Hg	75 ± 10	77 ± 10	78 ± 10	80 ± 11
Antihypertensive treatment	10	18	17	35
Body mass index, kg/m^2	25.7 ± 4.0	26.2 ± 3.9	28.2 ± 5.1	29.3 ± 4.4
Smoking	19	20	19	17
Diabetes	3	5	6	12
LV echocardiographic features				
LV mass (crude), g	147 ± 31	150 ± 25	201 ± 27	223 ± 39
Relative wall thickness	0.37 ± 0.04	0.47 ± 0.04	0.39 ± 0.03	0.49 ± 0.07
End-diastolic diameter, cm	4.80 ± 0.37	4.37 ± 0.30	5.26 ± 0.36	4.90 ± 0.31
Fractional shortening	0.36 ± 0.07	0.37 ± 0.07	0.36 ± 0.06	0.38 ± 0.06

Values are % for binary traits or mean ± SD for continuous traits.
BP = blood pressure; LV = left ventricular; n = number of observations.

eccentric hypertrophy dominates in this sample, the authors evaluated the change in LVEDD from baseline to follow-up in those participants who evolved from concentric to eccentric hypertrophy. As expected, the majority of participants (34 of 39; 87%) had an increase in LVEDD (Online Table 2).

CLINICAL CORRELATES OF CHANGE IN LV GEOMETRY. Increasing age, male sex, higher systolic BP, and greater BMI emerged as key correlates of abnormal LV geometry on follow-up (**Table 3**). Smoking and diabetes were also associated with increased odds of developing an abnormal LV geometric pattern, but only the association of diabetes with the development of concentric remodeling reached statistical significance. In those participants with an abnormal LV geometric pattern at baseline (concentric remodeling, concentric hypertrophy, and eccentric hypertrophy) (Online Table 3), male sex, older age, and higher level of BP and BMI at baseline were also associated with lower odds of reverting to normal geometry on follow-up. Thus, participants who were female, younger, and with lower systolic BP and BMI at baseline were more likely to revert to a normal LV pattern on follow-up (Online Table 3).

TABLE 2 Transition Rates of LV Geometric Pattern During a Mean Follow-Up of 4 Years

	LV Geometric Pattern on Follow-Up			
Baseline LV Geometric Pattern	Normal Geometry	Concentric Remodeling	Eccentric Hypertrophy	Concentric Hypertrophy
Normal geometry (n = 2,874)	68 (1,960)	20 (559)	8 (228)	4 (127)
Concentric remodeling (n = 820)	53 (437)	34 (279)	6 (47)	7 (57)
Eccentric hypertrophy (n = 590)	47 (274)	13 (78)	32 (189)	8 (49)
Concentric hypertrophy (n = 208)	29 (60)	17 (36)	19 (39)	35 (73)

Values are % (n).
LV = left ventricular; n = number of observations.

ASSOCIATION OF CHANGE IN LEFT VENTRICULAR GEOMETRY WITH INCIDENT CARDIOVASCULAR DISEASE (MYOCARDIAL INFARCTION, HEART FAILURE, AND DEATH FROM CORONARY HEART DISEASE). In this sample, there were 2,105 observations describing the change in LV geometry from examination cycles 5 to 6 (**Table 4**). Of these observations, 1,058 participants remained in the category of normal geometry or concentric remodeling (*referent* category), 439 participants *improved* and 479 *worsened*. Participants who remained in the concentric or eccentric hypertrophy group at cycle 6 (n = 129) (**Table 4**) were considered as a separate group as noted earlier. The median follow-up time was 12.0 years, and the total exposure time was 23,725.1 person-years. The unadjusted incidences of CVD (composite of myocardial infarction, heart failure, and death from CHD) were 4.2% (reference category), 7.1% (improved LV geometry), 9.0% (worsened LV geometry), and 17.1% (high-risk category) (**Table 5**). In age- and sex-adjusted models, worsening of the LV geometry was associated with an increased risk of CVD (**Table 5**).

As expected, participants who remained in the eccentric or concentric hypertrophy groups had the highest CVD risk. Analyses using ASE cut-points revealed comparable results (Online Table 4). Because of the relatively small number of participants (n = 129) and events (n = 22) (**Tables 4 and 5**), no subgroup analyses within the high-risk group could be performed.

DISCUSSION

PRINCIPAL FINDINGS. In this community-based cohort of middle-aged to older adults, the authors observed dynamic changes in LV geometry frequently. The key findings are summarized here. First, the proportion of participants who changed their LV geometric pattern depended on the baseline LV geometry. Two-thirds of participants with normal geometry at baseline remained in the same category, whereas only approximately one-third of participants with other geometric patterns remained in the same baseline category (diagonal in **Table 2**). Reversal to normal geometry was the most common change in participants with abnormal geometry at baseline. Second, in participants with normal geometry or concentric remodeling at baseline, progression to

TABLE 3 Multivariable-Adjusted ORs and 95% CIs for Different Geometric Pattern on Follow-Up for Participants With Normal LV Geometry at Baseline (2,874 Observations)*

Baseline Category	Category on Follow-Up						
		Concentric Remodeling		Concentric Hypertrophy		Eccentric Hypertrophy	
Normal Geometry	Normal	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Age, years	Referent	1.39 (1.24–1.56)	**<0.0001**	1.86 (1.48–2.34)	**<0.0001**	1.10 (0.93–1.31)	0.27
Male	Referent	1.12 (0.91–1.37)	0.28	3.25 (2.15–4.94)	**<0.0001**	1.35 (1.01–1.80)	**0.04**
Systolic BP, mm Hg	Referent	1.26 (1.10–1.43)	**0.0006**	1.72 (1.35–2.19)	**<0.0001**	1.39 (1.15–1.68)	**0.0007**
Body mass index, kg/m^2	Referent	1.01 (0.90–1.14)	0.82	2.01 (1.65–2.45)	**<0.0001**	1.74 (1.50–2.01)	**<0.0001**
Δ Systolic BP, mm Hg	Referent	1.05 (0.94–1.17)	0.43	1.28 (1.06–1.55)	**0.01**	1.18 (1.01–1.37)	**0.03**
Δ Body mass index, kg/m^2	Referent	1.03 (0.92–1.14)	0.65	1.18 (0.96–1.44)	0.11	1.12 (0.98–1.29)	0.10
Smoking status	Referent	1.26 (0.99–1.61)	0.059	1.26 (0.76–2.08)	0.38	1.21 (0.84–1.74)	0.30
Diabetes	Referent	1.84 (1.08–3.15)	**0.03**	1.51 (0.68–3.37)	0.31	1.39 (0.67–2.85)	0.38
Antihypertensive treatment	Referent	1.17 (0.85–1.61)	0.35	0.93 (0.54–1.58)	0.78	1.23 (0.79–1.90)	0.36

*OR per 1-SD increment in continuous traits and presence versus absence of binary traits. **Bold** indicates p values <0.05.
BP = blood pressure; CI = confidence interval; Δ = change from the baseline examination to the follow-up examination; OR = odds ratio.

concentric or eccentric hypertrophy was rare. Transition from eccentric to concentric hypertrophy was also relatively infrequent (8%), whereas progression from concentric to eccentric hypertrophy occurred in 19% of participants. Third, higher BP and greater BMI along with older age and male sex were the main clinical correlates of an adverse change in LV geometry. Fourth, the development of abnormal LV geometry was associated with increased risk of CVD on follow-up. The use of ASE-defined cut-points for LV geometric patterns (Online Tables 1 and 4) yielded results essentially similar to those obtained using empirical sex-specific percentiles for LVM and RWT.

IN THE CONTEXT OF THE LITERATURE. Pattern of change in left ventricular geometric pattern. Animal data parallel these findings supporting progression of LV geometry over time. Researchers noted that salt-sensitive Dahl rats fed a high-salt diet had an initial increase in LVM and RWT, followed by a decline in RWT after week 13 (19). These rats changed from concentric hypertrophy to eccentric hypertrophy and ultimately to symptomatic heart failure over the course of 20 weeks (11). Thus, there is substantial experimental evidence for a temporal sequence of concentric hypertrophy leading to eccentric hypertrophy and eventually to the development of clinical heart failure.

However, data in humans on the development of LV geometric pattern over time are relatively scarce and were predominantly derived from select subsamples of the population, such as patients with hypertension (20,21) or older patients (22), as detailed later.

Patients with hypertension and electrocardiographic evidence of LVH were part of the LIFE (Losartan Intervention For Endpoint reduction in hypertension) study, which reported the change in LV geometric pattern after 1 year of antihypertensive treatment (20). Consistent with the observations from the present analysis, progression from normal geometry or concentric remodeling to eccentric or concentric hypertrophy was rare in the LIFE study (20). Moreover, progression from concentric to eccentric hypertrophy was observed in approximately one-third of the moderately hypertensive patients in the LIFE sample (20), whereas this proportion was lower (19%) in this sample from the community. In line with the authors' observations, progression to eccentric hypertrophy was similarly relatively infrequent, and regression to normal geometry was

TABLE 4 Transition Matrix of LV Geometric Pattern From Examination Cycle 5 to Examination Cycle 6

Number of Observations	Examination Cycle 6				
	Normal Geometry	Concentric Remodeling	Eccentric Hypertrophy	Concentric Hypertrophy	Total
Examination cycle 5					
Normal geometry	915*	215†	112†	46†	1,288
Concentric remodeling	259‡	143*	33†	32†	467
Eccentric hypertrophy	92‡	18‡	87§	15†	212
Concentric hypertrophy	42‡	28‡	26†	42§	138
Total	1,308	404	258	135	2,105

*Participants with normal geometry or concentric remodeling at examinations 5 and 6 served as the referent category for the analyses relating change in LV geometry (from examination 5 to examination 6) to incident CVD (after examination 6). †A change to a more abnormal LV geometric pattern ("worsening"). ‡A change to a more normal LV geometric pattern ("improvement") over 4 years. §Participants with concentric hypertrophy or eccentric hypertrophy at examinations 5 and 6 were treated as a separate group ("remained high risk").

TABLE 5 Crude Event Rates, and Age- and Sex-Adjusted Hazard Ratios for Incident CVD/CHD Death (After Cycle 6) According to the Pattern of Change in LV Geometry (From Cycle 5 to 6)

Change in LV Geometry From Examination 5 to Examination 6	Events After Examination 6/ Participants at Risk	Risk (%)	Age- and Sex-Adjusted HR (95% CI)	p Value
Reference	44/1,058	4.2	1.00	
Improved	31/439	7.1	1.39 (0.88, 2.21)	0.16
Worsened	43/479	9.0	1.59 (1.04, 2.43)	0.03
High risk (remained EH/CH*)	22/129	17.1	3.42 (2.04, 5.74)	<0.0001

*Participants with eccentric hypertrophy at examination 5 and examination 6 or with concentric hypertrophy at examination 5 and examination 6.

CH = concentric hypertrophy; CHD = coronary heart disease; CI = confidence interval; CVD = cardiovascular disease; EH = eccentric hypertrophy; HR = hazard ratio; LV = left ventricular.

relatively common in older participants from the Cardiovascular Health Study (mean age 73 years) with concentric geometry at baseline (22). Thus, some evidence in these data supports a sequence (as described in experimental models) of a change from concentric remodeling to concentric hypertrophy and then to eccentric hypertrophy, even in the absence of interim CVD events. However, such a transition was observed in only a modest proportion of participants. It is also conceivable that transitions occurring during the 4-year period of follow-up may have been missed in this investigation.

Most participants who changed from concentric to eccentric hypertrophy in this sample displayed larger LVEDD on follow-up as compared with the baseline examination. This finding suggests that this change in LV geometry was likely driven by LV dilation.

Another interesting observation in the present data is that changes in LV geometry were relatively common when participants had abnormal baseline geometry. Only one-third of the participants with abnormal geometry remained in the same category (diagonal in **Table 2**). Approximately 29% to 53% of participants with abnormal geometry at baseline had normal geometry on follow-up. These findings are in agreement with results from the LIFE study (20), and they likely reflect the phenomenon of "regression to the mean" (23). Furthermore, they are consistent with the dynamic nature of LV geometry over time with the potential for reversibility.

Clinical correlates of changes in left ventricular geometric patterns. Overall, BP, BMI, age, and sex were the key correlates of change in LV geometry over the 4-year period. Older age, male sex, and higher baseline levels of BP and BMI were associated with increased odds of developing abnormal geometry on follow-up and with lower odds of regression to normal LV geometry. Among participants with abnormal LV geometry at baseline, those who were female, younger, and with lower systolic BP and BMI at baseline were more likely to revert to a normal LV pattern on follow-up (Online Table 3). These observations are in excellent agreement with data from cross-sectional and longitudinal studies on population-based samples (6,15,24–26). Overall, these data emphasize the importance of controlling CVD risk factors to prevent worsening of LV geometry and to reduce the associated risk of CVD.

Change in left ventricular geometry and risk of subsequent cardiovascular disease. Considerable evidence indicates that alterations in LV structure predict the incidence of heart failure and other forms of CVD (3,4,27–28). In an earlier report, Framingham investigators observed that participants with concentric hypertrophy, particularly men, had an increased risk of death and incident CVD. These associations were attenuated on adjustment for LVM and traditional risk factors (5). However, this latter report did not describe the pattern of change in LV geometry or the prognostic significance of *change* in LV geometry over time (5). In African Americans, concentric hypertrophy was strongly associated with diastolic dysfunction, whereas eccentric hypertrophy was strongly associated with systolic dysfunction in cross-sectional analyses (6). Similarly, higher LVM was associated with an increased risk of developing a reduced ejection fraction (<55%) on follow-up in older participants (age ≥65 years) from the community (29). When considering the LV geometric pattern in these participants, mainly eccentric LVH, but not concentric LVH, predicted the development of a low ejection fraction (29). In clinical samples of patients with concentric LVH at baseline, between 13% and 20% developed a reduced ejection fraction or systolic dysfunction during short-term follow-up (21,30,31). Consistent with the previously mentioned reports, the present analyses demonstrated that the development of an abnormal LV geometric pattern was associated with increased risk of subsequent CVD, including heart failure, myocardial infarction, and death from CHD. Even participants whose LV geometry improved over 4 years had an increased risk of subsequently developing CVD compared with the referent group (**Table 5** and Online Table 4), consistent with the notion that abnormal LV geometry in the past continues to confer an adverse prognosis.

STUDY LIMITATIONS. The strengths of this investigation include the availability of a large number of echocardiographic observations and the community-based, prospective design. Limitations include unavoidable biases resulting from differential

missingness and availability of echocardiographic data by baseline LV geometric pattern, regression to the mean, and misclassification caused by changes in the echocardiographic equipment over time and by intrareader temporal drift. However, the authors have implemented several quality control procedures in the echocardiography laboratory (as detailed in the Online Appendix) to monitor reproducibility of measurements and temporal trends in measurements.

The categorization of LV geometry is based on ratios of individual measurements that are sensitive to measurement error, and such error can lead to miscategorization. However, the authors expect this misclassification to be nondifferential (not related to LV geometry or incident CVD or death from CHD), thereby slightly reducing the statistical power of these analyses and less likely to introduce a systematic error.

Regardless of such factors, unfavorable changes in LV geometry were associated with an adverse prognosis. The generalizability of these observations to other ethnicities is unknown.

CONCLUSIONS

In this prospective study of a large community-based sample, the authors observed dynamic changes in LV geometry over a 4-year period and identified older age, male sex, higher BP, and greater BMI as key clinical correlates of such change. Worsening of LV geometry was associated with an adverse prognosis. Although observational, these findings provide support for the importance of control of CVD risk factors to prevent worsening of LV geometry and, in turn, reduce the risk of future CVD.

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KEY WORDS cardiovascular disease, change over time, echocardiography, epidemiology, heart failure, LV geometry, remodeling

APPENDIX For supplemental data, please see the online version of this article.