# Natural History of Concentric Left Ventricular Geometry in Community-Dwelling Older Adults Without Heart Failure During Seven Years of Follow-Up

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# Natural History of Concentric Left Ventricular Geometry in Community-Dwelling Older Adults without Heart Failure during Seven Years of Follow-up

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## Abstract

The presence of concentric left ventricular (LV) geometry has important pathophysiologic and prognostic implications. However, little is known about its natural history in older adults. Of the 5795 community-dwelling adults, ≥65 years, in the Cardiovascular Health Study, 1871 without baseline heart failure had data on baseline and 7-year echocardiography. Of these 343 (18%) had baseline concentric LV geometry (concentric remodeling, 83% and concentric LV hypertrophy, 17%) and are the focus of the current study. LV geometry at year 7 was categorized into 4 groups based on LV hypertrophy (LVH; LV mass indexed for height >51 g/m$^{2.7}$) and relative wall thickness (RWT): eccentric hypertrophy (RWT ≤0.42 with LVH), concentric hypertrophy (RWT >0.42 with LVH), concentric remodeling (RWT >0.42 without LVH), and normal (RWT ≤0.42 without LVH). At year 7, LV geometry normalized in 57%, remained unchanged in 35%, and transitioned to eccentric hypertrophy in 7% of participants. Incident eccentric hypertrophy occurred in 4% and 25% of those with baseline concentric remodeling and concentric hypertrophy respectively, and was associated with increased LV end-diastolic volume and decreased LV ejection fraction at year-7. Prior myocardial infarction and baseline above-median LV mass (>39 g/m$^{2.7}$) and RWT (>0.46) had significant unadjusted associations with incident eccentric LV hypertrophy; however, only LV mass >39 g/m$^{2.7}$ (odds ratio, 17.52; 95% CI, 3.91–78.47; p<0.001) and prior myocardial infarction (odds ratio, 4.73; 95% CI, 1.16–19.32; p=0.031) had significant independent associations. In conclusion, in community-dwelling older adults with concentric LV geometry, transition to eccentric hypertrophy was uncommon but structurally maladaptive.

### Keywords

concentric left ventricular remodeling; concentric left ventricular hypertrophy; eccentric left ventricular hypertrophy

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Concentric left ventricular (LV) geometry, defined by alterations in LV relative wall thickness (RWT) and LV mass, has important pathophysiologic and prognostic implications.[1, 2] Concentric remodeling commonly develops in response to chronically increased LV afterload caused by conditions such as arterial hypertension and aortic stenosis. On the contrary, eccentric hypertrophy commonly develops in response to chronically increased LV preload caused by conditions such as chronic mitral regurgitation. Heart failure (HF) patients may have either concentric or eccentric hypertrophy,[3] and it is unclear whether eccentric hypertrophy develops directly or progresses from concentric remodeling.

Findings from laboratory animals suggest that chronic pressure overload may lead to concentric hypertrophy with compensated LV function that over time progresses to eccentric hypertrophy, LV dilation, and decreased LV systolic function.[4] However, nearly half of all HF patients may have diastolic HF with normal LV ejection fraction and LV volume.[3, 5, 6] Most (≥ 90%) of these patients have antecedent hypertension and many (50–75%) have concentric geometry.[3, 5, 6] These observations led to the hypothesis that in humans, LV progression from concentric to eccentric geometry may not be common. However, this hypothesis has not been previously examined in those with LV concentric geometry without a history of HF. Furthermore, little is known about the natural history of LV concentric geometry. Therefore, the purpose of this prospective study was to examine the natural history of concentric LV geometry with a focus on its progression to eccentric hypertrophy.

## Methods

The Cardiovascular Health Study (CHS) is an ongoing epidemiologic study of cardiovascular disease in community-dwelling adults, ≥65 years, in the United States; the details of the rationale, design and implementation of which have been previously detailed.[7–9] Of the 5888 CHS participants, data on 5795 participants were available in the de-identified public-use copies of the datasets (93 participants declined to be included in these datasets). Of the 5795 CHS participants, 1871 were free of HF at baseline and also had data on echocardiography at baseline and at years 7.

LV hypertrophy (LVH) was defined as gender-neutral cutoff value for LV mass indexed for height >51 g/m$^{2.7}$.[10] RWT was computed by the ratio of sum of interventricular septal and posterior wall thickness to LV end-diastolic dimension. LV structure at baseline and year 7 was categorized as normal (RWT ≤0.42 and no LVH), concentric remodeling (RWT >0.42 and no LVH), concentric hypertrophy (RWT >0.42 and LVH) and eccentric hypertrophy (RWT ≤0.42 and LVH).[10] Of the 1871 CHS participants without baseline HF, 343 (18%) had LV concentric geometry who are the focus of the current study; of these 284 (83%) had concentric remodeling and 59 (17%) had concentric hypertrophy.

A multivariable logistic regression model was developed to identify baseline characteristics that predicted incident eccentric hypertrophy. In the model, LV mass indexed for height and LV RWT were categorized based on median values >39 g/m$^{2.7}$ and >0.46 respectively. The model was also adjusted for age, sex, race, baseline history of hypertension and prior acute myocardial infarction (AMI), and intercurrent (between baseline and year 7) AMI and HF. Because an intercurrent AMI may lead to eccentric hypertrophy via progressive remodeling with LV dilation and LV systolic dysfunction reflecting pathophysiology of coronary heart disease rather than hypertensive heart disease, we also repeated our analysis after excluding patients with intercurrent AMI.

## Results

Participants (n=343) had a mean (SD) age of 73 (5) years and a mean (SD) LV mass of 155 (51) grams, 63% were women, 8% were African American, and 59% had a history of hypertension (Table 1). At year 7, LV geometry normalized in 57% of participants, remained unchanged in 35%, and progressed to eccentric hypertrophy 7% of participants. Among those with LV concentric remodeling at baseline, LV geometry normalized in 63%, remained unchanged in 31%, progressed to concentric hypertrophy in 3% and eccentric hypertrophy in 4% of patients at year 7 (Table 2). Among those with LV concentric hypertrophy at baseline, LV geometry normalized in 29%, regressed to concentric remodeling in 24%, remained unchanged in 22%, and progressed to eccentric hypertrophy in 25% of patients at year 7 (Table 2).

Overall, 18 (5%) participants developed incident AMI during the 7 years of follow up, of whom 2 (11%) were found to have eccentric hypertrophy at year 7. Among those without incident AMI during the 7 years of follow up, incident eccentric hypertrophy at year 7 was observed overall in 7% (24/325) and in 27% (15/56) and 3% (9/269) participants with LV concentric remodeling and concentric hypertrophy respectively. Incident eccentric hypertrophy was associated with a higher prevalence of LV systolic dysfunction and a higher mean LV end-diastolic dimension (Table 2). Other echocardiographic findings at year 7 are displayed in Table 2. Incident HF occurred in 31 (9%) participants during 7 years of follow-up and of these, 4 (13%) had eccentric hypertrophy at year 7.

Prior AMI, height-indexed LV mass >39 $g/m^{2.7}$ and RWT >0.46 had significant unadjusted associations with incident eccentric LV hypertrophy (Table 3). However, after multivariable adjustment for other baseline characteristics, only LV mass >39 $g/m^{2.7}$ (odds ratio, 17.52; 95% CI, 3.91–78.47; p<0.001) and prior AMI (odds ratio, 4.73; 95% CI, 1.16–19.32; p=0.031) had significant independent associations (Table 3). These associations remained unchanged among participants without intercurrent AMI: LV mass >39 $g/m^{2.7}$ (odds ratio, 15.74; 95% CI, 3.49–70.90; p<0.001) and prior AMI (odds ratio, 4.22; 95% CI, 1.04–17.08; p=0.044) (data not presented in table). Associations of other baseline characteristics with incident eccentric hypertrophy among all participants are displayed in Table 3.

## Discussion

Findings from the current study demonstrate that the natural history of LV concentric geometry is dynamic in nature, and that over half regressed to or toward a more normal geometry and about a quarter did not change their LV geometry over 7 years of follow up. Regardless of an intercurrent AMI, only a small minority of patients with concentric remodeling and nearly a quarter of those with concentric hypertrophy developed eccentric hypertrophy. Prior AMI and baseline LV mass were significant independent predictors of progression from concentric geometry to eccentric hypertrophy.

The development of LV dilation and LV systolic dysfunction among older adults who developed eccentric hypertrophy at year 7 suggests that transition to eccentric geometry may be maladaptive. AMI is expected to cause progressive LV dilation and systolic dysfunction leading to eccentric hypertrophy. This is consistent with our findings of the association between prior AMI at baseline and development of eccentric hypertrophy at year 7. The lack of an association between intercurrent AMI and incident eccentric hypertrophy at year 7 may be due to small number of intercurrent AMI events and/or shorter time interval between intercurrent AMI and estimation of LV geometry at year 7.

The observation of a high rate of regression from a concentric to a normal LV geometry is rather intriguing, and it is tempting to attribute it to anti-hypertensive therapy as most of the

participants had a history of hypertension. However, LV geometry at year 7 among those with hypertension was similar (post hoc analysis: data not presented) regardless of the use of anti-hypertensive drugs. Finally, findings from our study suggest that in older adults with concentric LV geometry, LV mass is a stronger independent predictor of progression to eccentric hypertrophy than LV RWT. The prognostic importance of LV mass is also evident from the observation that the regression back to normal geometry was twice as common in older adults with concentric remodeling (RWT >0.42 without LVH) than in those with concentric hypertrophy (RWT >0.42 with LVH).

Several limitations of our study must be acknowledged. The findings of the current study are based on participants ≥65 years of age and thus may not be generalizable to younger populations. Further, because participants had to be alive during 7 years of follow-up for evaluation of LV geometry at year 7, a survivor cohort effect may have biased our findings resulting in a low rate of transition to eccentric geometry. However, findings from outcomes studies of LV geometry indicate that persistent concentric geometry rather than eccentric hypertrophy is more commonly associated with poor outcomes.[1, 11–13] Thus, it is unlikely that most of those who died during the 7 years of follow-up developed eccentric hypertrophy preceding their death. In conclusion, in community-dwelling older adults without HF and with concentric LV geometry at baseline, during 7 years of follow-up, most regressed to or toward a normal LV geometry and few transitioned to maladaptive eccentric hypertrophy.

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## Table 1

Baseline characteristics of older adults without heart failure and concentric left ventricular (LV) geometry at baseline and year 7 (n=343)

| Variable | n (%) or mean (±SD) |
|---|---|
| Age (years) | 73 (±5) |
| Female | 217 (63%) |
| African American | 26 (8%) |
| Smoking (pack years) | 16 (±25) |
| Height (cm) | 164 (±9) |
| Weight (pounds) | 155 (±28) |
| Body surface area ($m^2$) | 1.74 (±0.19) |
| Body mass Index ($kg/m^2$) | 26.1 (±3.9) |
| Systolic blood pressure (mmHg) | 137 (±23) |
| Diastolic blood pressure (mmHg) | 72 (±12) |
| Echocardiography | |
| LV systolic dysfunction* | 9 (3%) |
| LV fractional shortening (%) | 45 (±8) |
| LV end diastolic dimension (cm) | 4.3 (±0.5) |
| LV end diastolic interventricular septal thickness (cm) | 1.1 (±0.2) |
| LV end diastolic posterior wall thickness (cm) | 1.0 (±0.1) |
| LV mass (g) | 155.2 (±50.7) |
| Relative Relative wall thickness | 0.48 (±0.07) |
| Comorbidities | |
| Coronary heart disease | 50 (15%) |
| Prior myocardial infarction | 16 (5%) |
| Hypertension | 201 (59%) |
| Diabetes mellitus | 48 (14%) |
| LV hypertrophy (electrocardiogram) | 16 (5%) |
| Medications | |
| Angiotensin-converting enzyme inhibitors | 19 (6%) |
| Beta-blockers | 51 (15%) |
| Laboratory data | |
| Serum creatinine (mg/dL) | 0.91 (±0.28) |
| Serum cholesterol (mg/dL) | 2156 (±39) |
| Serum C-reactive protein (mg/dL) | 3.8 (±4.8) |

* Based on qualitative 2D echocardiography with estimated left ventricular ejection fraction <55%

## Table 2

LV geometry and other echocardiographic parameters at baseline and year 7 by their geometry at year 7*

| | **n (%) or mean (±SD)** | **Normal, n=178 (63%)** | | **Concentric remodeling, n= 87 (31%)** | | **Concentric hypertrophy, n= 8 (3%)** | | **Eccentric hypertrophy, n= 11 (4%)** | |
|---|---|---|---|---|---|---|---|---|---|
| | | **Year 0** | **Year 7** | **Year 0** | **Year 7** | **Year 0** | **Year 7** | **Year 0** | **Year 7** |
| Baseline concentric remodeling (n=284) | LV end-diastolic dimension (cm) | 4.2 (±0.4) | 4.7 (±0.5) | 4.1 (±0.4) | 4.1 (±0.4) | 4.3 (±0.5) | 5.0 (±0.5) | 4.5 (±0.3) | 5.5 (±0.5) |
| | LV mass (gram) | 141 (±32) | 132 (±33) | 133 (±35) | 137 (±35) | 151 (±53) | 236 (±67) | 157 (±26) | 205 (±27) |
| | LV fractional shortening (%) | 44.8 (±7.7) | 42.9 (±7.7) | 46.8 (±6.6) | 43.4 (±8.4) | 40.6 (±12.4) | 43.7 (±10.0) | 41.7 (±6.5) | 33.4 (±16.0) |
| | LV systolic dysfunction** | 3 (1%) | 6 (4%) | 3 (1%) | 4 (5%) | 1 (1%) | 2 (25%) | 2 (1%) | 4 (36%) |
| | n (%) or mean (±SD) | Normal, n=17 (29%) | | Concentric remodeling, n= 14 (24%) | | Concentric hypertrophy, n= 13 (22%) | | Eccentric hypertrophy, n= 15 (25%) | |
| | | Year 0 | Year 7 | Year 0 | Year 7 | Year 0 | Year 7 | Year 0 | Year 7 |
| Baseline concentric hypertrophy (n=59) | LV end-diastolic dimension (cm) | 5.0 (±0.3) | 5.1 (±0.4) | 4.6 (±0.5) | 4.1 (±0.4) | 5.1 (±0.6) | 4.8 (±0.3) | 4.8 (±0.4) | 5.5 (±0.6) |
| | LV mass (gram) | 222 (±41) | 164 (±35) | 218 (±44) | 167 (±32) | 251 (±60) | 238 (±45) | 233 (±59) | 229 (±60) |
| | LV fractional shortening (%) | 41.7 (±7.2) | 36.6 (±8.6) | 42.7 (±8.5) | 39.7 (±7.0) | 41.6 (±6.2) | 48.6 (±10.5) | 41.0 (±10.2) | 37.1 (±11.7) |
| | LV systolic dysfunction** | 1 (1%) | 4 (24%) | 1 (1%) | 1 (2%) | 1 (1%) | 0 (0%) | 3 (1%) | 6 (43%) |

* LV structure at year 7 was categorized as normal (RWT ≤0.42 and no LVH), concentric remodeling (RWT >0.42 and no LVH), concentric hypertrophy (RWT >0.42 and LVH) and eccentric hypertrophy (RWT ≤0.42 and LVH)

** Defined as LV ejection fraction <55% as qualitatively assessed on a baseline echocardiogram

## Table 3

Association of baseline characteristics with incident eccentric left ventricular (LV) hypertrophy in older adults with baseline concentric LV geometry

| Variable | Eccentric LV hypertrophy at year 7 | | Unadjusted odds ratio (95% CI); p value | Adjusted odds ratio (95% CI); p value |
|---|---|---|---|---|
| | No | Yes | | |
| Age ≥75 years | 105 (33%) | 10 (39%) | 1.26 (0.55–2.88); p=0.580 | 1.11 (0.46–2.69); p=0.823 |
| Female | 199 (63%) | 18 (9%) | 1.33 (0.56–3.16); p=0.513 | 1.94 (0.75–5.02); p=0.169 |
| African American | 24 (8%) | 2 (8%) | 1.02 (0.23–4.57); p=0.982 | 0.85 (0.18–4.05); p=0.840 |
| Hypertension | 147 (46%) | 16 (62%) | 1.85 (0.82–4.20); p=0.141 | 0.92 (0.38–2.25); p=0.856 |
| Previous acute myocardial infarction | 12 (4%) | 4 (15%) | 4.62 (1.38–15.52); p=0.013 | 4.73 (1.16–19.32); p=0.031 |
| Intercurrent acute myocardial infarction | 16 (5%) | 2 (8%) | 1.57 (0.34–7.22); p=0.564 | 2.22 (0.36–13.60); p=0.388 |
| Intercurrent heart failure | 27 (9%) | 4 (15%) | 1.95 (0.63–6.08); p=0.248 | 0.84 (0.22–3.24); p=0.800 |
| LV mass indexed for height >39* $g/m^{2.7}$ | 133 (42%) | 24 (92%) | 16.60 (3.88–71.46); p<0.001 | 17.52 (3.91–78.47); p<0.001 |
| Relative wall thickness >0.46* | 157 (50%) | 15 (58%) | 4.42 (1.60–12.18); p=0.004 | 1.09 (0.46–2.58); p=0.854 |

* Cutoffs based on median values