

BMJ Open Electrocardiography for the detection of left ventricular hypertrophy in an elderly population with long-standing hypertension in primary care: a secondary analysis of the CHELLO cohort study

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ABSTRACT

Objectives To investigate: (1) the prevalence of left ventricular hypertrophy (LVH) in elderly primary care patients with long-standing asymptomatic hypertension, and (2) the diagnostic value of ECG as a screening tool in the detection of LVH compared with echocardiography in this specific patient population.

Design and settings A cross-sectional study in five general practices in the south-east of the Netherlands.

Participants Patients with primary care-managed hypertension, aged between 60 and 85 years, without known heart failure.

Primary and secondary outcome measures Between June 2010 and January 2013, the patients underwent structured interviews, blood pressure assessment, laboratory testing, ECGs and echocardiograms. The primary outcome was to investigate the ability of ECG to detect LVH, compared with echocardiography as a reference test (gold standard).

Results Four hundred and twenty-two patients (44% male; ages 70±7 years) who underwent ECG and echocardiographic assessment to determine LVH were included. The median duration of hypertension was 10 (4–15) years. The overall prevalence of LVH was 44%, which increased with age ($p<0.001$); up to 60% of patients were ≥75 years. ECG intimated LVH in 47 patients (11%) but in only 26 of those (55%) was LVH confirmed by echocardiography. The sensitivity of ECG for detecting LVH was poor (14%).

Conclusions Asymptomatic primary care patients with long-standing hypertension have a high prevalence of previously undetected LVH, which increases with age. ECG is inadequate for detecting LVH in these patients. Early detection of LVH could potentially create more awareness for the optimal regulation of hypertension and compliance to therapy. Therefore, echocardiography should be considered a screening device for the detection of LVH in this population.

INTRODUCTION

Worldwide, hypertension is a common and increasingly frequent condition in the adult population.¹ A prevalence of up to 62% has been reported in the adult population of 60–70 years of age.² It is the most important

Strengths and limitations of this study

- In a primary care population of asymptomatic elderly individuals with long-standing hypertension: we report prevalence of left ventricular hypertrophy (LVH) by echocardiogram and the ability of ECG to detect this condition that has been associated with adverse outcomes.
- No long-term follow-up data on the occurrence of cardiac events are currently available, so adverse outcomes of LVH detected by ECG or echocardiography for future cardiovascular events remain unclear in this study,
- The design of the study has its limitations: it consists of a cross-sectional cohort without a control group for comparison.

(modifiable) risk factor for developing cardiovascular disease (CVD), including myocardial infarction (MI), stroke, atrial fibrillation and heart failure.³ Clinical findings related to hypertensive heart disease include left ventricular hypertrophy (LVH), secondary left ventricular (LV) diastolic dysfunction and left atrial dilation. LV diastolic dysfunction is a well-known cause of heart failure, leading to high morbidity and mortality.⁴ The detection of LVH is important because these patients' risk of cardiovascular (CV) morbidity and mortality is twofold to fourfold increased, compared with patients with normal LV mass.⁵

Most patients with hypertension are diagnosed in primary care. The first choice of treatment is lifestyle and dietary interventions, followed by drug therapy. Achieving adequate blood pressure control is pivotal in reducing the risks of hypertension-mediated organ damage. In the Netherlands, general practitioners treat patients according to the

latest nationwide guidelines for CV risk management.⁶ However, these guidelines are conservative in their recommendations for additional testing after laboratory and blood pressure assessments. Standard ECG and echocardiography are not recommended in these guidelines to screen for, among other things, LVH. In particular, in long-standing hypertension with known high morbidity and mortality, LVH should be recognised using the most reliable method available,⁷ in order to intensify the regulation of blood pressure so that LVH can be modified in time.^{8,9} This will hopefully increase patient awareness and adherence to therapy.

Moreover, the value of ECG screening in primary care patients with hypertension has not yet been fully explained. The increase in myocardial wall thickness is the most apparent finding with regard to end-organ damage due to uncontrolled hypertension and elevated pressure load.¹⁰ This may first be noted by ECG, using specific criteria,¹¹ however, the sensitivity to diagnose LVH in a general population is low, in comparison to echocardiography as the reference gold standard.^{12,13} In primary care, though, ECG is still the preferred tool in patients with hypertension, since it is easy to obtain, fast and inexpensive. With the increasing accessibility of ultrasound machines to primary care physicians, it is important to decide whether ECG remains a viable tool as first choice for detecting LVH, or perhaps in selected patients only. It is conceivable that in patients with longer duration of hypertension, having a higher incidence and higher rates of severe LVH due to chronic pressure overload,¹⁴ ECG may still have a diagnostic role.

The aim of the current study was to investigate: (1) the prevalence of LVH in elderly primary care patients with long-standing asymptomatic hypertension, and (2) the diagnostic value of electrocardiography as a screening tool in the detection of LVH compared with echocardiography in this specific patient population.

METHODS

Study design and patient population

This study was performed using data from the CHELLO (Chronic Heart Failure Prevention Program) study. The details of this study have been presented earlier.^{15–17} In summary, between June 2010 and January 2013, a total of 913 primary care patients aged between 60 and 85 years with an International Classification of Primary Care for hypertension (K86/K87) were invited from five general practices affiliated with the primary care organisation Praktijkondersteuning Zuidoost Brabant to participate in the CHELLO study.

Inclusion criteria were: elderly primary care patients (60–85 years) with asymptomatic hypertension. Patients with a history of CVD (eg, MI) were included if they were no longer treated by a cardiologist. Exclusion criteria: patients with heart failure were excluded based on nature of the primary study (Chronic Heart Failure Prevention Program).

Other exclusion criteria included: severe psychiatric illness other than mood or anxiety disorders; serious cognitive impairment; terminal cancer; insufficient knowledge of the Dutch language; or illiteracy. This resulted in 595 eligible patients who gave written informed consent for participation.

Patient and public involvement

No patient involved.

Study procedure and data collection

Eligible patients received both verbal and written information on the study. After obtaining written informed consent, an interview was scheduled at the primary care practice. During this first visit, a healthcare nurse conducted a structured interview and performed a physical examination. Blood pressure was measured automatically after approximately 20 and 40 min, with the patient in a sitting position. The mean value of both blood pressure measurements was used for data analysis. In addition, demographic and clinical variables were obtained during the interview and after reviewing the patient's medical records. Following the first appointment, blood was drawn by venipuncture in order to measure brain natriuretic peptide (BNP), total cholesterol and low-density lipoprotein. BNP was measured since it is a known indicator of heart failure, which could be the result of long-term LVH.^{3,18} A follow-up visit was planned at the primary care practice in order to perform an ECG and echocardiogram.

Assessment of the ECG and echocardiogram

The primary outcome was to investigate the ability of ECG to detect LVH, compared with echocardiography as a reference test (gold standard).

ECG and echocardiogram were carried out by a trained, experienced echocardiographer at the local primary care laboratory 'Diagnostiek voor U' in Eindhoven, the Netherlands.

A standard resting 12-lead ECG was recorded (paper speed 25 mm/s, 10 mm/mV). We used the following eight well-known and often used criteria in order to evaluate the LVH features during ECG:

- ▶ The Sokolow-Lyon index: the sum of the S wave in V1 and the R wave in V5 or V6 >3.5 mV.¹⁹
- ▶ The sum of the S wave in V2 and the R wave in V5 or V6 >4.5 mV.²⁰
- ▶ The amplitude of the R wave in V5 or V6 >2.6 mV.¹⁹
- ▶ A comparison of the amplitude of the R wave in V5 and V6; R V6 > R V5.²¹
- ▶ The sum of the largest amplitude of the R wave and the largest amplitude of the S wave in precordial leads >4.5 mV.²²
- ▶ The Cornell voltage: the sum of the R wave in augmented vector left (aVL) and the S wave in V3 >2.0 mV for females and >2.8 mV for males.²³
- ▶ The amplitude of the R wave in aVL >1.1 mV.¹⁹

- ▶ The Gubner-Ungerleider voltage: the sum of the R wave in I and the S wave in the III lead >2.5 mV.²⁴

If one or more of these eight criteria were positive, ECG-LVH was diagnosed. An independent cardiologist who was blinded for outcomes of the echocardiogram gave a final review.

A transthoracic 2D echocardiographic examination was performed with an s5 transducer (Philips CX 50) in a standard position. All the echocardiograms were reviewed by a panel of cardiologists specialised in echocardiography, according to European recommendations and guidelines for evaluating chamber quantification, diastolic dysfunction and heart valve disease.^{25–27} LVH was defined as any abnormal LV size measurement (septal or posterior wall thickness >0.9 cm in females or >1.0 cm in males) and calculated LV mass index adjusted for body surface area >95 g/m² in females and >115 g/m² in males. We used Cube formula for LV mass = $0.8 * 1.04 * [(IVS + LVID + PWT)^3 - LVID^3] + 0.6$ g.²⁶

Statistical analyses

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences V.25.0. Data are presented as mean \pm SD in the case of normally distributed data, median (interquartile interval) for non-normally distributed data and number (percentage) for nominal data. A p value <0.05 (two tailed) was considered to indicate statistical significance.

In order to examine the prevalence of LVH, we calculated the proportion of patients with echocardiography-diagnosed LVH. In addition, we computed the 95% CI for this estimate. In order to examine the diagnostic yield of ECG, we calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with a 95% CI. McNemar's test was used to compare LVH detection rates between ECG and echocardiography in 2x2 contingency tables. In addition, the kappa measure of agreement value was calculated.

To assess a potential effect of age on our result, we divided our population (n=422) into four groups: group 1 (n=116) less than 65 years old; group 2 (n=102) 65–69 years old; group 3 (n=102) 70–74 years old; group 4 (n=102) 75 years and older.

In order to assess the discriminative ability of ECG, we compared the demographic, lifestyle and clinical characteristics of patients without LVH and patients with LVH. Characteristics were compared using an independent samples t-test for normally distributed continuous data, the Mann-Whitney U test for non-normally distributed continuous data and the χ^2 test for categorical data. In the same way, the discriminative ability of echocardiograms was assessed.

Finally, in order to investigate whether the ECG, together with other demographic and clinical variables, can be used as a proxy for the echocardiogram when diagnosing LVH, we performed single and subsequent multiple logistic regression analyses with LVH (normal \pm abnormal) using the echocardiogram as the dependent variable. The

multivariable logistic regression model was constructed using backward selection ($p_{out} > 0.1$), including variables that were significantly associated with LVH on the echocardiogram in univariable analyses.

RESULTS

Study population

A total of 427 patients from the CHELLO study cohort (595), with both an ECG and an echocardiogram, were included. Five patients were excluded due to the poor image quality of the echocardiogram, resulting in a total of 422 eligible patients.^{15–17}

Baseline characteristics

Table 1 presents the baseline characteristics of the study participants. The mean age of these patients was 69.7 ± 6.5 years, with the minority being male (44%, n=186). The median years of hypertension amounted to 10 [4–15] years. Mean systolic blood pressure (SBP) was 149.2 ± 20.2 mm Hg, and mean diastolic blood pressure was 81.8 ± 10.8 mm Hg. In all the patients, 67% had an SBP >140 mm Hg (n=281), and as much as 44% an SBP >150 mm Hg (n=185). Therefore, in this population, 42% (n=175) had an SBP that was on target according to the Dutch guidelines for CV risk management. On-target SBP was defined as <140 mm Hg for those aged less than 70 years and <150 mm Hg for those aged 70 years or older.⁶

Prevalence and diagnostic yield of LVH using ECG compared with echocardiography

The overall prevalence of LVH using echocardiogram was 44% (n=184), while that of LVH using ECG was 11% (n=47).

Of the 422 patients, 47 (11%) had LVH using ECG and, of these 47 patients, 26 (55%) had LVH confirmed using echocardiography. In other words, in almost half of those patients with LVH detected using ECG, this was not confirmed by echocardiography.

ECG had a sensitivity of 14% (95% CI 9.44% to 20.02%), a specificity of 91% (95% CI 86.83% to 94.46%), a PPV of 56% (95% CI 41.86% to 68.04%) and an NPV of 58% (95% CI 56.13% to 59.58%) for the detection of LVH using echocardiography.

Detection of LVH using ECG was not associated with LVH using echocardiography based on McNemar's test ($p < 0.001$). There was poor agreement between ECG and echocardiogram used for the detection of LVH (kappa 0.058, $p = 0.086$). A typical example of LVH mismatch is demonstrated in figure 1.

Prevalence of LVH in different age categories using ECG and echocardiogram

The prevalence of LVH using ECG increased with increasing age, however not significantly ($\chi^2(3) = 5.06$, $p = 0.17$). The prevalence of LVH using echocardiography increased significantly with increasing age ($\chi^2(3) = 18.58$, $p < 0.001$). Figure 2 shows the distribution of LVH using ECG and echocardiography in the four different age categories.

Table 1 Baseline characteristics

Characteristic	Total patients n=422
Demographics	
Age (mean, SD)	69.7±6.5
Male (n, %)	186 (44.1)
Low education (n, %)	53 (12.6)
Having a partner (n, %)	327 (77.5)
Lifestyle	
Current smoker (n, %)	54 (12.8)
Regular alcohol use (n, %)*	135 (32.0)
Recommended physical exercise (n, %) [†]	68 (16.1)
Clinical characteristics and risk factors	
Previous MI (n, %)	19 (4.5)
Peripheral artery disease (n, %)	18 (4.3)
Previous TIA/stroke (n, %)	36 (8.5)
Diabetes (n, %)	39 (9.2)
BMI (mean, SD) [‡]	28±4.6
BNP (median, IQR) [§]	10(6–18)
Total cholesterol (mean, SD) [¶]	5.1±1.0
LDL (mean, SD)	3.1±0.9
SBP (mean, SD)	149±20.2
SBP >140 (n, %)	281 (66.6)
SBP >150 (n, %)	185 (43.8)
DBP (mean, SD)	81.8±10.8
DBP >90 (n, %)	86 (20.4)
Blood pressure on target (n, %)**	175 (41.5)
Years of hypertension (median, IQR) [¶]	10(4–15)

Values for categorical variables are given as number (percentage); values for continuous variables are given as mean±SD or median (IQR).

*Defined as ≥2 glasses of alcohol per day on average.

[†]Defined as ≥30 min exercise per day, at least five 5 days/week.

[‡]n=418.

[§]n=400.

[¶]n=407 due to missing data.

**On-target systolic blood pressure defined as <140 mm Hg for persons aged less than 70 years and <150 mm Hg for persons aged 70 years or more.

BMI, body mass index; BNP, brain natriuretic peptide; DBP, diastolic blood pressure; LDL, low-density lipoprotein; MI, myocardial infarction; SBP, systolic blood pressure; TIA, transient ischaemic attack.

The prevalence of LVH confirmed by echocardiography increased from 33% in the youngest age group (<65 years) to 60% in the oldest age group (>74 years), while the prevalence of LVH using ECG only increased from 11% in the youngest age group to 18% in the oldest age group.

Study characteristics with regard to LVH status using ECG and echocardiogram

Table 2 presents patient characteristics with regard to LVH using ECG and echocardiogram.

LVH was only significantly correlated with age using the echocardiogram; patients with LVH by echocardiography were older when compared with those without LVH (71±6.9 vs 69±6.0, $t(420)=-4.29$, $p<0.001$). BNP was significantly higher in those with LVH on both ECG (17 (9.9–31) vs 9.7 (5.8–16.3), $U=5132$, $z=-4.08$, $p<0.001$, $r=0.20$) and echocardiography (11 (6.9–18) vs 9.8 (5.3–17), $U=17220$, $z=-2.11$, $p=0.035$, $r=0.11$) when compared with those without LVH. An elevated BNP was more strongly associated with LVH when using ECG than when using the echocardiogram.

Furthermore, only SBP was significantly higher in those with LVH using ECG compared with those without LVH (155±23.1 vs 149±19.7, $t(420)=-1.82$, $p=0.041$). Moreover, an SBP >150 mm Hg was significantly higher in those with LVH compared with those without LVH using ECG (60% vs 42%, $\chi^2(1)=5.32$, $p=0.021$).

With regard to the echocardiogram, patients with LVH were more likely to have had a previous MI compared with those without LVH (7% vs 3%, $\chi^2(1)=4.98$, $p=0.026$). Moreover, the body mass index (BMI) was significantly higher in those with LVH using echocardiography compared with those without LVH (29±4.3 vs 28±4.7, $t(416)=-2.03$, $p=0.043$). Lastly, SBP was significantly higher in those with LVH on the echocardiogram, compared with those not suffering from LVH (152±21.7 vs 147±18.7, $t(420)=-2.69$, $p=0.007$).

Predictors of LVH

Table 3 presents the results from univariable and multivariable logistic regression analysis, with an abnormal echocardiogram LVH as the dependent variable. In univariable logistic regression analysis, greater age, previous MI, higher BMI, higher BNP, higher SBP and LVH on ECG were associated with echocardiogram-diagnosed LVH. After backward elimination, in multivariable logistic regression analysis, only greater age (OR 1.06, 95% CI 1.03 to 1.10), previous MI (OR 2.86, 95% CI 1.04 to 7.83) and higher BMI (OR 1.05, 95% CI 1.01 to 1.10) were found to be predictors of echocardiogram-diagnosed LVH.

DISCUSSION

In this cross-sectional study of elderly asymptomatic primary care patients with long-standing hypertension, we found a prevalence of LVH of 44% using echocardiography. The prevalence of LVH detected with echocardiography increased significantly with age: up to 60% in patients older than 75 years. We also investigated the value of ECG in the detection of LVH compared with our findings with echocardiography. ECG had a poor predictive value to detect LVH, with a low sensitivity of 14%. In contrary to our echocardiography findings, we did not find an increase in prevalence of ECG-detected LVH with increasing age, prevalence stabilised at around 16%–18% in the highest age group. Early detection and subsequent treatment of LVH are important in an effort to reduce CV

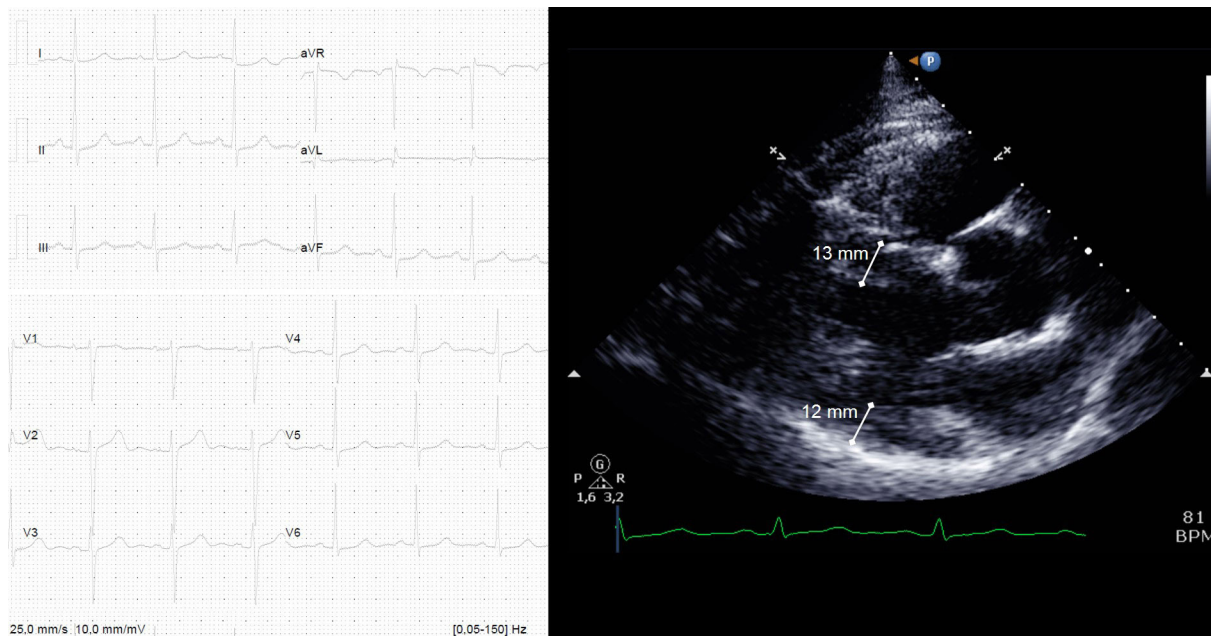


Figure 1 Normal ECG and abnormal echocardiogram of LVH in one patient. aVF, augmented vector foot; aVL, augmented vector left; aVR, augmented vector right; LVH, left ventricular hypertrophy.

morbidity and mortality,²⁸ even in patients older than 65 years.²⁹ Since most patients with hypertension are treated in primary care setting, there is a need for an easy, affordable and reliable screening tool to detect LVH in this population.

Strengths and limitations

In this study we evaluated the prevalence of LVH using echocardiography in a specific primary care cohort of asymptomatic elderly individuals with long-standing hypertension. Furthermore, we compared the ability of ECG to detect LVH with echocardiography as a reference test.

We conclude that there should be a standard role for echocardiography when screening for LVH in primary care patients with hypertension.

One of the limitations of this study is that we used a cross-sectional design, without a control group for comparison. Furthermore, this study unfortunately lacks any long-term data on (cardiac) events, so adverse outcomes of LVH detected by ECG or echocardiography for the development of future CV events remain unclear in this population.

Comparison with the existing literature

The prevalence of echocardiographically confirmed LVH in the general population is estimated to be from 14% to 19%, and increases with age.^{30,31} In our study, in a selected primary care patient population with long-standing hypertension, we noted a higher prevalence of LVH of 44%. This corresponds with the prevalence of LVH reported in a recent review by Cuspidi *et al*, who noted a variation from 36% to 41% in patients with hypertension.³² Only limited data of prevalence of LVH in elderly primary care patients with hypertension are available. Doroudi *et al* reported a prevalence of LVH of 38% in patients in primary care, aged between 62 and 73, but this is a retrospective study.³³ Chowdhury *et al* report a prevalence of LVH detected by the echocardiogram of 33%–70%, depending on used definition. Although our reported prevalence of LVH detected with echocardiography (44%) fits within this range, the study of Chowdhury *et al* did not comment on the value of ECG in detecting LVH in their population.³⁴

The Framingham study pointed out that the use of ECG for detecting LVH in the general population was not reliable.¹² They reported that ECG has a sensitivity of less than 20% for detecting LVH compared with echocardiography. When using cardiac MRI, Bacharova *et al* also reported the poor sensitivity (22%) of ECG for detecting LVH in the general population.³⁵ In a review of Pewsner

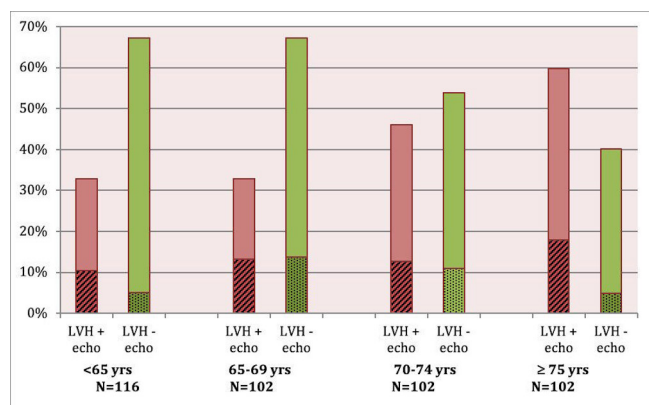


Figure 2 Prevalence of LVH using echocardiography and ECG (%) in different age categories. Light red: LVH– ECG. Striped dark red: LVH+ ECG. Light green: LVH– ECG. Dotted dark green: LVH+ ECG. LVH, left ventricular hypertrophy.

Table 2 Characteristics according to LVH using ECG and echocardiogram

Characteristics	ECG n=422		P value	ECHO n=422		P value
	LVH+ n=47	LVH- n=375		LVH+ n=184	LVH- n=238	
Demographics						
Age (mean, SD)	70.9±6.4	69.5±6.5	0.166	71.2±6.9	68.5±6.0	<0.001
Male (n, %)	23 (48.9)	163 (43.5)	0.476	83 (45.1)	103 (43.3)	0.707
Low education (n, %)	5 (10.6)	48 (12.8)	0.673	24 (13.0)	29 (12.2)	0.792
Having a partner (n, %)	37 (78.7)	290 (77.3)	0.830	141 (76.6)	186 (78.2)	0.711
Lifestyle						
Current smoker (n, %)	4 (8.5)	50 (13.3)	0.351	19 (10.3)	35 (14.7)	0.182
Regular alcohol use (n, %)*	14 (29.8)	121 (32.3)	0.731	61 (33.2)	74 (31.1)	0.653
Recommended physical exercise (n, %) [†]	8 (17.0)	60 (16.0)	0.858	28 (15.2)	40 (16.8)	0.660
Clinical characteristics and risk factors						
Previous MI (n, %)	2 (4.3)	17 (4.5)	0.931	13 (7.1)	6 (2.5)	0.026
Peripheral artery disease (n, %)	1 (2.1)	17 (4.5)	0.442	5 (2.7)	13 (5.5)	0.166
Previous TIA/stroke (n, %)	1 (2.1)	35 (9.3)	0.096	20 (10.9)	16 (6.7)	0.130
Diabetes (n, %)	4 (8.5)	35 (9.3)	0.854	19 (10.3)	20 (8.4)	0.499
BMI (mean, SD) [‡]	27±4.0	28±4.6	0.178	29±4.3	28±4.7	0.043
BNP (median, IQR) [§]	17 (9.9–31)	9.7 (5.8–16.3)	<0.001	11.0 (6.9–18)	9.8 (5.3–17)	0.035
Total cholesterol (mean, SD) [¶]	5.2±1.1	5.1±1.0	0.522	5.1±1.1	5.0±0.9	0.286
LDL (mean, SD) [¶]	3.2±0.9	3.1±0.9	0.746	3.2±0.9	3.1±0.9	0.361
SBP (mean, SD)	155±23.1	149±19.7	0.041	152±21.7	147±18.7	0.007
SBP >140 (n, %)	33 (70.2)	248 (66.1)	0.576	128 (69.6)	153 (64.3)	0.254
SBP >150 (n, %)	28 (59.6)	157 (41.9)	0.021	89 (48.4)	96 (40.3)	0.099
DBP (mean, SD)	83.7±10.9	81.6±10.7	0.203	81±10.9	82±10.6	0.188
DBP >90 (n, %)	11 (23.4)	75 (20.0)	0.585	36 (19.6)	50 (21.0)	0.715
Blood pressure on target (n, %)**	15 (31.9)	160 (42.7)	0.158	71 (38.6)	104 (43.7)	0.291
Years of hypertension (median, IQR) [¶]	10 (4–15)	10 (4–16)	0.629	10 (4–20)	8 (4–15)	0.188

Values for categorical variables are given as number (percentage); values for continuous variables are given as mean±SD or median (IQR). χ^2 test for nominal data, t-test for normally distributed continuous data, Mann-Whitney U test for non-normally distributed data. P values <0.05 are in bold.

*Defined as ≥ 2 glasses of alcohol per day on average.

[†]Defined as ≥ 30 min exercise per day, at least 5 days/week.

[‡]n=418.

[§]n=400.

[¶]n=407 due to missing data.

**On-target systolic blood pressure defined as <140 mm Hg for persons aged less than 70 years and <150 mm Hg for persons aged 70 years or more.

BMI, body mass index; BNP, brain natriuretic peptide; DBP, diastolic blood pressure; ECHO, echocardiogram; LDL, low-density lipoprotein; LVH, left ventricular hypertrophy; MI, myocardial infarction; SBP, systolic blood pressure; TIA, transient ischaemic attack.

et al, the studies in hypertensive primary care populations reported a median sensitivity ranged from 8.5% to 21%.³⁶ Furthermore, in another large study Jain *et al* found a similar sensitivity range of 5.7%–26% for detecting LVH with ECG in a hypertensive population compared with MRI.³⁷ We hypothesised that the reliability of ECG may be better in a selected group of patients with long-standing hypertension, which could be helpful in primary care practice. Unfortunately, our data show that ECG performed equally poor, even in this specific population.

Although our results have shown that ECG may not be recommended for the detection of LVH, the prognostic value of ECG in elderly primary care patients with hypertension remains uncertain. It has been hypothesised that ECG may be of additional value for prognosis.^{7 38 39} Aro and Chugh suggested that LVH detected using ECG and LVH detected using echocardiography are two distinct entities that only partially overlap, and have different prognostic significance⁴⁰ (see [figure 3](#)). This hypothesis could explain the stronger association of elevated BNP

Table 3 Univariable and multivariable association of LVH using echocardiogram with clinical parameters in patients with asymptomatic hypertension

	LVH on echocardiogram			
	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Demographics				
Higher age	1.07 (1.04 to 1.10)	<0.001	1.06 (1.03 to 1.10)	0.001
Male	0.93 (0.63 to 1.37)	0.707		
Low education	1.08 (0.61 to 1.93)	0.792		
Having a partner	0.92 (0.58 to 1.45)	0.711		
Lifestyle				
Current smoker	0.66 (0.37 to 1.21)	0.184		
Regular alcohol use*	1.10 (0.73 to 1.66)	0.653		
Recommended physical exercise†	0.89 (0.53 to 1.50)	0.660		
Clinical characteristics and risk factors				
Previous MI	2.94 (1.10 to 7.89)	0.032	2.86 (1.04 to 7.83)	0.041
Peripheral artery disease	0.48 (0.17 to 1.38)	0.175		
Previous TIA/stroke	1.69 (0.85 to 3.37)	0.134		
Diabetes	1.26 (0.65 to 2.43)	0.500		
Higher BMI‡	1.05 (1.00 to 1.09)	0.046	1.05 (1.01 to 1.10)	0.032
LnBNP§	1.35 (1.06 to 1.71)	0.014		
Higher total cholesterol¶	1.12 (0.91 to 1.37)	0.278		
Higher LDL¶	1.11 (0.89 to 1.38)	0.360		
Higher SBP	1.01 (1.00 to 1.02)	0.008		
SBP >140	1.27 (0.84 to 1.92)	0.255		
SBP >150	1.39 (0.94 to 2.04)	0.099		
Higher DBP	0.99 (0.97 to 1.01)	0.188		
DBP >90	0.92 (0.57 to 1.48)	0.715		
Blood pressure on target**	1.24 (0.84 to 1.83)	0.291		
More years of hypertension¶	1.15 (0.94 to 1.41)	0.170		
LVH on ECG	1.70 (0.92 to 3.13)	0.088		

Data are presented as OR with corresponding p value. Bold numbers indicate a p value <0.1 at univariable analysis, and p value <0.05 at multivariable analysis.

*Defined as ≥ 2 glasses of alcohol per day on average.

†Defined as ≥ 30 min exercise per day, at least 5 days/week.

‡n=418.

§n=400.

¶n=407 due to missing data.

**On-target systolic blood pressure defined as <140 mm Hg for persons aged less than 70 years and <150 mm Hg for persons aged 70 years or more.

BMI, body mass index; DBP, diastolic blood pressure; LDL, low-density lipoprotein; LnBNP, log-transformed brain natriuretic peptide; LVH, left ventricular hypertrophy; MI, myocardial infarction; SBP, systolic blood pressure; TIA, transient ischaemic attack.

with LVH using ECG as opposed to LVH using echocardiogram. The current study was unable to address this further.

Implications for research and/or practice

Our results provide additional proof that routinely acquired ECGs for detecting LVH in patients with hypertension have no significant diagnostic value, not even in a selected population with long-standing hypertension. On

the other hand, ECG-derived LVH seems, at least partly, to be a different entity and a predictor of CV mortality, independent of LV mass index and LV morphology. Moreover, ECG-LVH increases the risk of CV mortality even in subjects without hypertension.^{41 42} Routinely performing both ECG and echocardiography in patients with hypertension seems therefore indicated. Currently, both our national and European guidelines for CV risk management (in

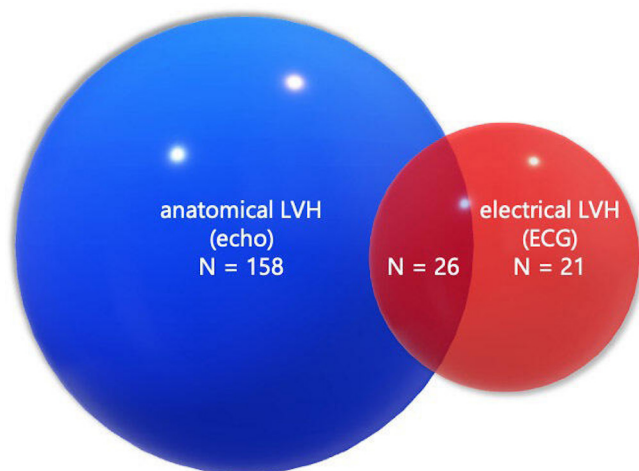


Figure 3 Anatomical versus electrical left ventricular hypertrophy (LVH) (adapted from Aro and Chugh [40] pointing out anatomical and electrical LVH, and their overlap, in our study).

primary care) do not recommend routinely performance of an ECG and/or echocardiogram.

Our findings point out that, when feasible, patients (particularly uncomplicated elderly patients with hypertension, who represent a large percentage of the population) should be referred for focused echocardiography for detection of LVH.⁴³ Performing an ECG could be of additional prognostic value, independent of echocardiographic findings.^{7 38–42}

Furthermore, our study showed that more than half the patients were not on target with their blood pressure, and it is possible that early recognition of LVH will increase patient awareness and adherence to therapy. Also, the early detection of LVH will identify patients who could benefit from intensified antihypertensive therapy, in order to prevent or delay the progression of CVD.^{28 29 44–47}

In conclusion, asymptomatic, elderly primary care patients with long-standing hypertension have a high prevalence of LVH, which will increase with age. ECG is a suboptimal tool for detecting LVH and, for this reason, patients who are in need of close monitoring and stricter antihypertensive treatment may benefit from a cardiac evaluation with echocardiography. Further follow-up exploration is required to prove the prognostic value of ECG and echocardiography in this specific population of primary care patients with hypertension. Moreover, future research should concentrate on whether the early detection of LVH by echocardiography in the primary care setting leads to decreased morbidity and mortality in the increasing prevalence of hypertension.

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REFERENCES

- Egan BM, Zhao Y, Axon RN. Us trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. *JAMA* 2010;303:2043–50.
- Blokstra A, Vissink P, Venmans L. Nederland de Maat Genomen 2012;27.
- Williams B, Mancia G, Spiering W, *et al.* 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018;39:3021–104.
- Bleumink GS, Knetsch AM, Sturkenboom MCJM, *et al.* Quantifying the heart failure epidemic: prevalence, incidence rate, lifetime risk and prognosis of heart failure the Rotterdam study. *Eur Heart J* 2004;25:1614–9.
- Katholi RE, Couri DM. Left ventricular hypertrophy: major risk factor in patients with hypertension: update and practical clinical applications. *Int J Hypertens* 2011;2011:495349.
- Dis VI, Henstra Y, Den Hertog H, *et al.* The NHG-Guideline cardiovascular risk management (second update). huisarts wetenschap 2019.
- Cuspidi C, Facchetti R, Sala C, *et al.* Do combined electrocardiographic and echocardiographic markers of left ventricular hypertrophy improve cardiovascular risk estimation? *J Clin Hypertens* 2016;18:846–54.
- Dahlöf B, Devereux RB, Kjeldsen SE, *et al.* Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension study (life): a randomised trial against atenolol. *Lancet* 2002;359:995–1003.
- Stewart MH, Lavie CJ, Shah S, *et al.* Prognostic implications of left ventricular hypertrophy. *Prog Cardiovasc Dis* 2018;61:446–55.
- Marwick TH, Gillebert TC, Aurigemma G, *et al.* Recommendations on the use of echocardiography in adult hypertension: a report from the European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE)†. *Eur Heart J Cardiovasc Imaging* 2015;28:727–54.
- Surawicz B, Childers R, Deal BJ, *et al.* AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part III: intraventricular conduction disturbances: a scientific statement from the American heart association electrocardiography and arrhythmias Committee, Council on clinical cardiology; the American College of cardiology Foundation; and the heart rhythm Society: endorsed by the International Society for computerized Electrocardiology. *Circulation* 2009;119:e235–40.
- Levy D, Garrison RJ, Savage DD, *et al.* Prognostic implications of echocardiographically determined left ventricular mass in the Framingham heart study. *N Engl J Med* 1990;322:1561–6.

- 13 Haider AW, Larson MG, Benjamin EJ, *et al.* Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. *J Am Coll Cardiol* 1998;32:1454–9.
- 14 Levy D, Anderson KM, Savage DD, *et al.* Echocardiographically detected left ventricular hypertrophy: prevalence and risk factors. The Framingham heart study. *Ann Intern Med* 1988;108:7–13.
- 15 Ringoir L, Widdershoven JW, Pedersen SS, *et al.* Symptoms associated with an abnormal echocardiogram in elderly primary care hypertension patients. *Neth Heart J* 2014;22:234–9.
- 16 Ringoir L, Pedersen SS, Widdershoven JW, *et al.* Beta-blockers and depression in elderly hypertension patients in primary care. *Fam Med* 2014;46:447–53.
- 17 Ringoir L, Pedersen SS, Widdershoven JW, *et al.* Prevalence of psychological distress in elderly hypertension patients in primary care. *Neth Heart J* 2014;22:71–6.
- 18 Ponikowski P, Voors AA, Anker SD, *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;37:2129–200.
- 19 Sokolow M, Lyon TP. The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. *Am Heart J* 1949;37:161–86.
- 20 Romhilt DW, Bove KE, Norris RJ, *et al.* A critical appraisal of the electrocardiographic criteria for the diagnosis of left ventricular hypertrophy. *Circulation* 1969;40:185–96.
- 21 Holt DH, Spodick DH. The Rv6:Rv5 voltage ratio in left ventricular hypertrophy. *Am Heart J* 1962;63:65–6.
- 22 McPhie J. Left ventricular hypertrophy: electrocardiographic diagnosis. *Australas Ann Med* 1958;7:317–27.
- 23 Casale PN, Devereux RB, Alonso DR, *et al.* Improved sex-specific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: validation with autopsy findings. *Circulation* 1987;75:565–72.
- 24 Gubner R. Electrocardiographic criteria of left ventricular hypertrophy. *Arch Intern Med* 1943;72:196–209.
- 25 Galderisi M, Cosyns B, Edvardsen T, *et al.* Standardization of adult transthoracic echocardiography reporting in agreement with recent chamber quantification, diastolic function, and heart valve disease recommendations: an expert consensus document of the European association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging* 2017;18:1301–10.
- 26 Lang RM, Badano LP, Mor-Avi V, *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of echocardiography and the European association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging* 2015;16:233–71.
- 27 Nagueh SF, Smiseth OA, Appleton CP, *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of echocardiography and the European association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging* 2016;17:1321–60.
- 28 Go AS, Mozaffarian D, Roger VL, *et al.* Heart disease and stroke statistics--2013 update: a report from the American Heart Association. *Circulation* 2013;127:e6–245.
- 29 Milan A, Caserta MA, Avenatti E, *et al.* Anti-hypertensive drugs and left ventricular hypertrophy: a clinical update. *Intern Emerg Med* 2010;5:469–79.
- 30 Schirmer H, Lunde P, Rasmussen K. Prevalence of left ventricular hypertrophy in a general population; the Tromsø study. *Eur Heart J* 1999;20:429–38.
- 31 Levy D, Savage DD, Garrison RJ, *et al.* Echocardiographic criteria for left ventricular hypertrophy: the Framingham heart study. *Am J Cardiol* 1987;59:956–60.
- 32 Cuspidi C, Sala C, Negri F, *et al.* Prevalence of left-ventricular hypertrophy in hypertension: an updated review of echocardiographic studies. *J Hum Hypertens* 2012;26:343–9.
- 33 Doroudi S, DeLisi MD, DeBari VA. A review of echocardiograms in hypertensive patients greater than 60 years in a community based family medicine program. *J Community Hosp Intern Med Perspect* 2017;7:28–33.
- 34 Chowdhury EK, Jennings GLR, Dewar E, *et al.* Predictive performance of echocardiographic parameters for cardiovascular events among elderly treated hypertensive patients. *Am J Hypertens* 2016;29:821–31.
- 35 Bacharova L, Chen H, Estes EH, *et al.* Determinants of discrepancies in detection and comparison of the prognostic significance of left ventricular hypertrophy by electrocardiogram and cardiac magnetic resonance imaging. *Am J Cardiol* 2015;115:515–22.
- 36 Pewsner D, Jüni P, Egger M, *et al.* Accuracy of electrocardiography in diagnosis of left ventricular hypertrophy in arterial hypertension: systematic review. *BMJ* 2007;335:711.
- 37 Jain A, Tandri H, Dalal D, *et al.* Diagnostic and prognostic utility of electrocardiography for left ventricular hypertrophy defined by magnetic resonance imaging in relationship to ethnicity: the multi-ethnic study of atherosclerosis (MESA). *Am Heart J* 2010;159:652–8.
- 38 Patel N, O'Neal WT, Whalen SP, *et al.* Electrocardiographic left ventricular hypertrophy predicts atrial fibrillation independent of left ventricular mass. *Ann Noninvasive Electrocardiol* 2017;22:e12419–5.
- 39 Bacharova L, Schocken D, Estes EH, *et al.* The role of ECG in the diagnosis of left ventricular hypertrophy. *Curr Cardiol Rev* 2014;10:257–61.
- 40 Aro AL, Chugh SS. Clinical diagnosis of electrical versus anatomic left ventricular hypertrophy: prognostic and therapeutic implications. *Circ Arrhythm Electrophysiol* 2016;9:e003629.
- 41 Brown DW, Giles WH, Croft JB. Left ventricular hypertrophy as a predictor of coronary heart disease mortality and the effect of hypertension. *Am Heart J* 2000;140:848–56.
- 42 Tanaka K, Tanaka F, Onoda T, *et al.* Prognostic value of electrocardiographic left ventricular hypertrophy on cardiovascular risk in a non-hypertensive community-based population. *Am J Hypertens* 2018;31:895–901.
- 43 Bornemann P, Johnson J, Tiglaos S, *et al.* Assessment of primary care physicians' use of a pocket ultrasound device to measure left ventricular mass in patients with hypertension. *J Am Board Fam Med* 2015;28:706–12.
- 44 Devereux RB, Wachtell K, Gerds E, *et al.* Prognostic significance of left ventricular mass change during treatment of hypertension. *JAMA* 2004;292:2350–6.
- 45 Franz IW, Tönnemann U, Müller JF. Time course of complete normalization of left ventricular hypertrophy during long-term antihypertensive therapy with angiotensin converting enzyme inhibitors. *Am J Hypertens* 1998;11:631–9.
- 46 Fagard RH, Celis H, Thijs L, *et al.* Regression of left ventricular mass by antihypertensive treatment: a meta-analysis of randomized comparative studies. *Hypertension* 2009;54:1084–91.
- 47 Klingbeil AU, Schneider M, Martus P, *et al.* A meta-analysis of the effects of treatment on left ventricular mass in essential hypertension. *Am J Med* 2003;115:41–6.