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Title: Association between self-reported hypertension onset age and electrocardiographic left ventricular hypertrophy

Running title: Self-reported hypertension onset age and ECG-LVH

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Abstract

Objectively defined early-onset hypertension, based on repeated blood pressure measurements, is associated with greater odds of organ damage and cardiovascular mortality than late-onset hypertension. In this study we examined the association between two factors that are easily available in primary care, self-reported hypertension onset age and electrocardiographic left ventricular hypertrophy (ECG-LVH), in a nationwide population sample of 2864 Finns aged ≥50 years. We observed that, in contrast to prior findings, the odds of ECG-LVH were similar between self-reported hypertension onset age groups, and thus self-reported early-onset hypertension does not seem to associate with ECG-LVH more strongly than simple presence of hypertension.

Keywords

Hypertension, early-onset hypertension, blood pressure, electrocardiography, left ventricular hypertrophy

Introduction

Hypertension present at either younger or older age increases the risk of cardiovascular disease. However, prior studies suggest that hypertension that *begins* at an early age, assessed with repeated blood pressure (BP) measurements, is more strongly associated with cardiovascular mortality and hypertension-mediated organ damage (HMOD) than late-onset hypertension [1-5]. However, data from repeated BP measurements spanning decades may not be available in everyday clinical practice and physicians have to rely on self-reported hypertension onset age. In addition, assessment of HMOD according to guidelines in primary care is often limited to electrocardiographic left ventricular hypertrophy (ECG-LVH) and urinary albumin excretion [6,7]. Further research on whether self-reported hypertension onset age is associated with ECG-LVH is therefore warranted.

In this study, we examined the association of self-reported hypertension onset age and ECG-LVH in a nationwide population sample of 2864 Finns aged ≥50 years in 2000–2001. Our aim was to investigate whether ECG-LVH is more common in individuals with self-reported early- versus late-onset hypertension.

Methods

In 2000–2001, 8032 Finns >30 years were randomly drawn from the population register and invited to participate in the Health 2000 survey [8]. Of the 6354 who participated, we excluded participants aged <50 years (n=2950) so that all participants could be classified into all age-of-onset categories. We also excluded individuals with paced rhythm, Wolf-Parkinson-White pattern, atrial fibrillation, ventricular conduction defect, or missing covariates for a final study sample of 2864 individuals. The Health 2000 Survey was performed according to the Declaration of Helsinki and was approved by the local ethical committee. All participants provided informed consent.

Standard 12-lead ECGs were recorded using a MAC 5000 recorder (Marquette Hellige, Freiburg, Germany, and Milwaukee, Wisconsin, USA) and analyzed with Magellan software (Marquette Electronics Inc., Milwaukee, Wisconsin, USA). All ECGs were Minnesota coded by two cardiologists blinded to clinical status. In the case of disagreement (28% of all ECGs), final coding was decided through consensus. ECG-LVH was defined using Sokolow-Lyon voltage (SV1+RV5/V6 ≥3.5 mV), Cornell voltage (SV3+RaVL >2.8 mV for men and >2.0 mV for women), and Minnesota code (codes 3.1/3.3) criteria.

Hypertension onset age (i.e., the year when hypertension had been diagnosed) was self-reported at the health interview. We divided the participants into categories by hypertension onset age (<40 years, 40–49 years, ≥50 years, or no hypertension).

The study participants provided comprehensive information about their medical history to interviewers. Fasting blood samples, height and weight were obtained during the health examination. Diabetes was defined as fasting glucose ≥7.0 mmol/l or use of antidiabetics. BP values were defined as means of two BP measurements with a mercury sphygmomanometer.

We compared ECG-LVH prevalence across groups using a X^2 test. We used univariable and multivariable logistic regression models to evaluate the association between hypertension onset age groups and ECG-LVH, with those who did not report hypertension as the referent group. We compared the differences in odds ratios for ECG-LVH between hypertension onset at <40 years and ≥50 years using a *z* test. Models were adjusted for age, sex, BMI, smoking, diabetes, non-HDL-cholesterol, heart rate, heart failure, coronary heart disease, use of antihypertensive medication and systolic BP. We also assessed the multivariable-adjusted odds ratios of ECG-LVH after excluding participants on renin–angiotensin–aldosterone system inhibitors (n=350). We considered two-tailed $P<0.05$ as statistically significant.

Results

The characteristics of the study sample are shown in **Table 1**. In the whole sample, 1158 participants (40%) had self-reported hypertension and 801 individuals (28 %) used antihypertensive medication. The prevalence of ECG-LVH by Sokolow-Lyon voltage, Cornell voltage, and Minnesota code criteria was significantly higher in participants with hypertension compared with those without ($P \leq 0.0001$ for all). We observed no significant difference in the prevalence of ECG-LVH between hypertension onset age groups ($P \geq 0.47$ for all).

Table 1. presents the odds of ECG-LVH by hypertension onset age group. Hypertension onset at any age was related to increased odds ratios (OR) of ECG-LVH based on the Sokolow-Lyon and Minnesota criteria ($P < 0.001$ for both). However, compared with participants without hypertension, hypertension onset at age <40 years and ≥50 years was associated with similar odds of ECG-LVH by Sokolow-Lyon voltage criteria (OR, 2.10; 95% confidence interval [CI], 1.19-3.72 versus OR, 2.00; 95% CI, 1.39-2.87; P=0.95). The findings were comparable for Cornell voltage (OR, 1.17; 95% CI, 0.66-2.08 versus OR, 1.05; 95% CI, 0.72-1.53, P=0.89) and Minnesota code criteria (OR, 2.22; 95% CI, 1.40-3.52 versus OR, 1.57; 95% CI, 1.15-2.15; P=0.60), respectively. The results were similar when participants on renin–angiotensin–aldosterone system inhibitors (n=350) were excluded (data not shown).

Discussion

In this study, we demonstrate that the odds of ECG-LVH were not greater in individuals with self-reported early-onset hypertension compared with individuals with late-onset hypertension. Thus, self-reported hypertension onset age does not seem to offer incremental value over simple presence of hypertension when assessing the odds of ECG-LVH.

Major guidelines for the management and treatment of hypertension recommend assessing ECG-LVH from all hypertensive patients for evaluating presence of HMOD [6,7]. Indeed, ECG-LVH is a well-known marker of cardiovascular risk and its regression improves prognosis independent of BP [9]. Here, we observed that the odds of ECG-LVH were similar in participants with self-reported early-onset hypertension compared with participants with late-onset hypertension. Although we observed a modest trend for an association between hypertension onset age and ECG-LVH defined by Minnesota code criteria, our results somewhat contrast previous findings on the stronger association of objectively defined early- versus late-onset hypertension with coronary artery calcification, echocardiographic LVH, and diastolic dysfunction [4]. In addition to using a less accurate self-report, instead of repeated BP measurements, for defining hypertension onset age, an alternative reason for our results could be that the sensitivity of ECG-LVH for detecting anatomical LVH is only moderate [10].

Recent data from cohort studies suggest that objectively defined early-onset hypertension is a stronger predictor of cardiovascular mortality than late-onset hypertension [1-3]. It is important to note that the previous studies have determined hypertension onset age objectively with precise and carefully documented BP measurements [2]. However, the extent to which *self-*

reported hypertension onset age is associated with cardiovascular outcomes remains less studied. Only one study with 2649 middle-aged participants has shown that self-reported onset at <35 years was associated with echocardiographic LVH, diastolic dysfunction, and coronary calcification, whereas onset at ≥45 years was only associated with diastolic dysfunction [11]. Self-reported information on hypertension onset age could therefore still be useful for physicians who treat hypertensive patients without objective long-term BP data. However, our results imply that hypertension onset age may not be particularly useful in estimating the odds of ECG-LVH when hypertension onset age is assessed by self-report.

Strengths of our study include a relatively large and representative study sample and availability of ECG-LVH that was assessed both manually and with computerized software. However, we did not have information available on the duration or intensity of antihypertensive treatment. Additionally, during the Health 2000 Survey, the most common BP threshold for initiating antihypertensive treatment in Finland was ≥160/100 mmHg as recommended by then-current guidelines [12].

We conclude that early-onset hypertension does not seem to associate with ECG-LVH more strongly than simple presence of hypertension. However, considering recent evidence on early-onset hypertension being an important predictor of adverse cardiovascular outcomes, we advocate the value of assessing hypertension onset age in hypertensive patients in order to identify high-risk individuals and to prevent hypertensive complications.

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Conflict of Interest

The authors declare no conflict of interest.

Summary Table

What is known about this topic?

- Objectively defined early-onset hypertension, based on repeated blood pressure measurements, is related to cardiovascular outcomes.
- The relation between self-reported age of hypertension onset and electrocardiographic left ventricular hypertrophy (ECG-LVH) has remained unknown.

What this study adds?

- Self-reported hypertension onset at any age is related to increased odds of ECG-LVH.
- Odds of ECG-LVH, however, were similar between hypertension onset age groups.
- Self-reported early-onset hypertension does not seem to associate with ECG-LVH more strongly than simple presence of hypertension.

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Table 1. Sample characteristics and odds of ECG-LVH according to self-reported hypertension onset age.

		Self-reported age of hypertension onset				
Characteristic/Odds	All	< 40 y	40-49 y	≥50 y	Hypertension onset at any age	No hypertension
N	2864	172	329	657	1158	1706
Age, years (SD)	63.2 (10.2)	59.2 (7.0)	59.4 (8.5)	67.0 (9.5)	63.7 (9.7)	62.9 (10.5)
No women (%)	1639 (57.2)	98 (57.0)	160 (48.6)	409 (62.2)	666 (57.5)	973 (57.0)
BMI, kg/m² (SD)	27.8 (4.6)	29.8 (5.1)	28.8 (4.7)	28.7 (4.5)	28.9 (4.7)	27.1 (4.4)
Current smoker (%)	537 (18.8)	33 (19.2)	70 (21.3)	92 (14.0)	195 (16.8)	342 (20.0)
Non-HDL cholesterol, mmol/l (SD)	4.9 (1.1)	5.0 (1.2)	4.9 (1.1)	4.8 (1.1)	4.9 (1.1)	4.9 (1.1)
Heart rate, n/min (SD)	63.4 (10.8)	64.2 (11.3)	63.4 (11.1)	63.1 (10.9)	63.4 (11.0)	63.5 (10.7)
Diabetes (%)	313 (10.9)	25 (14.5)	42 (12.8)	103 (15.7)	170 (14.7)	143 (8.4)
Systolic blood pressure, mmHg (SD)	143 (21.5)	152 (21.1)	148 (20.2)	153 (21.2)	151 (21.0)	138 (20.1)
Diastolic blood pressure, mmHg (SD)	83.2 (11.2)	88.5 (10.1)	88.2 (10.5)	85.0 (12.1)	86.4 (11.5)	81.0 (10.4)
Use of antihypertensive medication (%)	801 (28.0)	124 (72.1)	207 (62.9)	444 (67.6)	775 (66.9)	26 (1.5)
Use of ACEi or ARB (%)	350 (12.2)	55 (32.0)	96 (29.2)	173 (26.3)	324 (28.0)	26 (1.5)
Hormone replacement therapy (%)*	468 (28.6)	35 (35.7)	41 (25.6)	108 (26.5)	184 (27.6)	284 (29.2)
Coronary disease (%)	318 (11.1)	28 (16.3)	49 (14.9)	97 (14.8)	174 (15.0)	144 (8.4)
Heart failure (%)	160 (5.6)	12 (7.0)	23 (7.0)	49 (7.5)	84 (7.3)	76 (4.5)
Stroke (%)	104 (3.6)	12 (7.0)	15 (4.6)	31 (4.7)	58 (5.0)	46 (2.7)
Sokolow-Lyon LVH (%)	310 (10.8)	21 (12.2)	41 (12.5)	95 (14.5)	157 (13.6)	153 (9.0)
Cornell LVH (%)	357 (12.5)	24 (14.0)	46 (14.0)	109 (16.6)	179 (15.5)	178 (10.4)
Minnesota LVH (%)	485 (17.0)	40 (23.3)	69 (21.0)	143 (21.8)	252 (21.8)	233 (13.7)
Odds for LVH (95% CI)						
Sokolow-Lyon		2.10 (1.19-3.72)	1.81 (1.16-2.83)	2.00 (1.39-2.87)	1.95 (1.41-2.72)	1.00 (ref)
Cornell		1.17 (0.66-2.08)	1.35 (0.85-2.14)	1.05 (0.72-1.53)	1.13 (0.79-1.61)	1.00 (ref)
Minnesota		2.22 (1.40-3.52)	1.78 (1.22-2.58)	1.57 (1.15-2.15)	1.69 (1.27-2.25)	1.00 (ref)

*In women (N=1639). BMI, body mass index; HDL, high density lipoprotein; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker, Sokolow-Lyon LVH, left ventricular hypertrophy by Sokolow-Lyon voltage criteria; Cornell LVH, left ventricular hypertrophy by Cornell voltage criteria; Minnesota LVH, left ventricular hypertrophy by Minnesota code; CI, confidence interval. Odds ratios were adjusted for age, sex, BMI, smoking, diabetes, non-HDL-cholesterol, heart rate, heart failure, coronary heart disease, use of antihypertensive medication, and systolic blood pressure.