### ORIGINAL ARTICLE

# The association between ECG criteria and Echo criteria for left ventricular hypertrophy in a general Chinese population

Tingting Lv<sup>1</sup> | Yifang Yuan<sup>2</sup> | Jing Yang<sup>1</sup> | Guijin Wang<sup>3</sup> | Lingyun Kong<sup>1</sup> | Huijuan Li<sup>2</sup> | Xingjie Li<sup>4</sup> | Yingxian Sun<sup>5</sup> | Xuewen Li<sup>6</sup> | Zheng Zhang<sup>7</sup> | Xiaoshu Cheng<sup>8</sup> | Lirong Wu<sup>9</sup> | Xuerui Tan<sup>10</sup> | Bing Han<sup>11</sup> | Hua Li<sup>1</sup> | Zhaoguo Zhang<sup>12</sup> | Jiayu Wang<sup>13</sup> | Yangfeng Wu<sup>2</sup> | Yanfang Wang<sup>2</sup> | Jihong Guo<sup>13</sup> | Ping Zhang<sup>1</sup>

<sup>1</sup>Department of Cardiology, Tsinghua University, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Beijing, China

<sup>2</sup>Peking University, Clinical Research Institute, Beijing, China

<sup>4</sup>Department of Cardiology, Jining NO. 1 People's Hospital, Jining, China

<sup>5</sup>Department of cardiology, First Affiliated Hospital of China Medical University, Shenyang, China

<sup>6</sup>Department of cardiology, Shanxi Academy of medical sciences, Shanxi Dayi Hospital, Taiyuan, China

<sup>7</sup>Department of Cardiology, The First Hospital of Lanzhou University, Lanzhou, Gansu, China

<sup>8</sup>Department of Cardiology, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, China

<sup>9</sup>Department of cardiology, The Affiliated Hospital of Guiyang Medical College, Guiyang, China

<sup>10</sup>Department of Cardiology, The First Affiliated Hospital of Shantou University Medical College, Shantou, China

<sup>11</sup>Department of cardiology, Xuzhou Central Hospital, Xuzhou, China

<sup>12</sup>Department of cardiology, First Hospital of Integrated Chinese and Western Medicine, Beijing, China

<sup>13</sup>Department of cardiology, People's Hospital of peking University, Beijing, China

#### Correspondence

Ping Zhang, Department of Cardiology, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China. Email: zhpdoc@126.com

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# Abstract

**Background:** Several ECG criteria have been widely used for diagnosis of left ventricular hypertrophy (LVH) in clinical practice. However, their performance in a general Chinese population is limited.

**Methods and results:** A multi-stage, stratified cluster sampling across China was performed and 7415 representative Chinese adults aged 18–85 years were analyzed. ECG was collected by using GE MAC 5500 machine. The association between five ECG-LVH criteria (i.e., Peguero–Lo Presti, Cornell, Cornell product, Sokolow–Lyon and Sokolow–Lyon product) and echocardiographic LVH (Echo-LVH) was assessed by *Pearson's* correlation, diagnostic statistics like predictive values, and receiver operating characteristics (ROC) curve. We found that the prevalence of the Echo-LVH was 11% while ECG-LVH ranged from 3% to 27%. All ECG-LVH criteria had high negative predictive value (NPV) (89%) and specificity (73–96%) but low positive predictive

Tingting Lv and Yifang Yuan contributed equally to this work.

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<sup>&</sup>lt;sup>3</sup>Department of electronic engineering, Tsinghua University, Beijing, China

value (PPV) (12–24%) and sensitivity (4–29%). The newly Peguero–Lo Presti criteria had higher sensitivity (29%) but lower specificity (73%) and accuracy (68%) compared with other criteria. Cornell product had the best diagnostic performance (AUC: 0.59), as well as the highest specificity (96%) and accuracy (86%) but lowest sensitivity (4%). Among single-lead components of ECG criteria,  $R_{aVL}$  voltage and QRS duration performed relatively better than others. Hypertensive and older individuals had higher sensitivity but lower specificity and accuracy than their counterparts.

**Conclusion:** ECG-LVH criteria had high NPV to detect Echo-LVH. Though with higher sensitivity, Peguero-Lo Presti criteria did not have better diagnostic performance to detect Echo-LVH.  $R_{aVL}$  and QRS duration had stronger association with Echo-LVH among all single-lead components.

#### KEYWORDS

ECG, echocardiography, hypertension, left ventricular hypertrophy

# 1 | INTRODUCTION

Left ventricular hypertrophy (LVH), which is defined by increased left ventricular mass (LVM), is usually regarded as a response to chronic pressure and volume load, and it has been reported as an independent risk factor for subclinical atherosclerosis and heart failure (Bayml & Underwood, 2014; Drazner et al., 2004; Velagaleti et al., 2014; Zile et al., 2011) with a prevalence of up to 15%–20% in the general population (Weber, 1991). Cardiac magnetic resonance imaging (MRI) is the current gold standard for evaluation of LVH (Jain et al., 2010). Nevertheless, two-dimensional echocardiography is still the main routine tool to estimate LV mass in clinical practice given economic considerations (Palmieri et al., 1999). In clinical practice, ECG is so far the most cost-effective and convenient tool to screen for LVH, and great efforts have been made to improve the performance of ECG-LVH criteria over the years.

Researchers have proposed numerous ECG criteria to evaluate LVH, with a high specificity of 85%-90% but low sensitivity of less than 50%, and different criteria often have different sensitivity, specificity, and accuracy (Hancock et al., 2009). Among the various criteria, Sokolow-Lyon and Cornell criteria were more commonly used in clinical practice (Sokolow et al., 2004; Casale et al., 1987). And it has been often reported that Sokolow-Lyon voltage criteria have higher sensitivity while Cornell voltage criteria have higher specificity. The product of QRS duration and voltage derived from Sokolow-Lyon or Cornell criteria were reported to be more accurate than the voltage alone (Khaled et al., 2004). Recently, Peguero et al. reported that sum voltage of the deepest S wave  $(S_d)$  and S wave in lead V4  $(S_{V4})$ outperformed Cornell voltage with a significantly higher sensitivity (Peguero et al., 2017). Most validation of these ECG-LVH criteria was conducted in Caucasians from Europe and United States of America. Furthermore, some studies presented that there was racial difference between Whites and African Americans with ECG-LVH (Chapman et al., 1999; Peter et al., 2017). However, the validation and comparison of these ECG-LVH in a Chinese general population were limited.

In our present study, we aimed to analyze the association between ECG-LVH and LVH diagnosed by two-dimensional echocardiography (Echo-LVH) in a general Chinese population. We also explored if the results differed by age, body mass index (BMI), and blood pressure in a Chinese population.

# 2 | METHODS

### 2.1 | Study design and study population

We used data from China National Survey of ECG Measures, a crosssectional study conducted in China during 2012–2013. In this national survey, a multi-stage, stratified cluster sampling method was applied to select study participants. First, we classified 31 provinces, autonomous regions, and municipalities in mainland China into eight geographic regions. One administrative area from each region was then selected by convenience, with consideration of their representativeness of the regional social and economic development status. Then, a stratified cluster random sampling was used to select about 1000 eligible study participants in each of the eight regions, half from urban and half from rural. More detailed study design was described in all study participants were provided with detailed information, and data collection started after the informed consent form was signed. The study was reviewed and approved by the Peking University People's Hospital Institution Review Board (#2012–17).

For this analysis, we additionally excluded the following participants: 1) participants absence of echocardiogram or ECG; 2) participants with poor-quality ECG; 3) participants with non-sinus rhythm, including atrial fibrillation, atrial flutter, junctional rhythm, et al; 4) participants with frequent premature ventricular contraction or aberration; 5) participants with major ventricular conduction abnormalities, such as complete left or right bundle branch blocks, QRS duration  $\geq$ 120 ms; 6) participants with S wave area <160  $\mu$ V·ms in all leads.

# 2.2 | Electrocardiography

Standard 12-lead ECGs were digitally acquired at a sampling rate of 2000 samples per second using GE MAC 5500 ECG machine (GE Healthcare, Wauwatosa, Wisconsin) by trained technicians and stored using the MUSE data management system for later retrieval. All ECGs were auto-analyzed using a GE/Marquette 12lead ECG Analysis Program-12SL (GE Healthcare) at a central core laboratory.

ECG-LVH was defined based on the following ECG-LVH criteria which were calculated from the automatically measured ECG waveforms and mainly used in clinical practice:

- 1. Peguero-Lo Presti voltage: deepest S wave in any single-lead  $S_D + S_{V4} \ge 2.3 \text{ mV}$  for women and  $\ge 2.8 \text{ mV}$  for men (Peguero et al., 2017)
- 2. Sokolow–Lyon voltage:  $S_{V1} + R_{V5/V6} \ge 3.5 \text{ mV}$  (Casale et al., 1987)
- 3. Gender-specific Cornell voltage:  $S_{V3} + R_{aVL} > 2.8$  mV for men and >2.0 mV for women (Casale et al., 1987)
- 4. Cornell voltage product:  $(R_{aVL} + S_{V3})$  \* QRS duration ≥244 000 µV·ms (Molloy et al., 1992)
- 5. Sokolow-Lyon voltage product:  $(S_{V1} + R_{V5/V6})^*QRS$  duration  $\geq$ 371 000 µV·ms (Molloy et al., 1992)

# 2.3 | Echocardiography

Echocardiography examinations were performed by trained researchers following standard protocols. End-diastolic interventricular septum (IVSd), posterior wall thickness (PWTd), and left ventricular internal diameter (LVIDd) were obtained by twodimensional echocardiography-guided M-mode tracings. Left ventricular mass (LVM) was estimated by cube formula 0.8 × 1.0  $4 \times [(IVSd + LVIDd + PWTd)^3 - LVIDd^3] + 0.6$  g,, and left ventricular mass index (LVMI) was LVM indexed by body surface area (BSA) calculated as 0.007184 × Height<sup>0.725</sup> × Weight<sup>0.425</sup> reported by Devereux et al (Devereux et al., 1986). Cutoff values of LVMI as Echo-LVH were defined as 115 g/m<sup>2</sup> for male and 95 g/m<sup>2</sup> for female according to American Society of Echocardiography (Recommendations, 2016).

# 2.4 | Covariates

Standard questionnaires were used to collect information about demographics, socioeconomic, medical and family history, medication use, smoking, alcohol intakes, and physical activity. Physical examinations following standard protocol were used for anthropometry and blood pressure measurement. Seated blood pressure was measured three times with a calibrated upper arm electronic monitor. Average blood pressure was analyzed in the study. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg.

# 2.5 | Statistical analysis

We first described the baseline characteristics according to LVH group and non-LVH groups. Numerical variables were reported as mean ± standard deviation for normal-distributed variables and median (25%, 75%) for non-normal-distributed variables. Categorical variables were reported as percentages. We then analyzed Pearson correlation between LVMI and the voltage or voltage product of ECG-LVH. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were reported to describe the performance of each ECG-LVH criteria. AUC analysis was used to evaluate the discrimination ability of ECG-LVH criteria to identify Echo-LVH. McNemar's test was used to compare these ECG-LVH criteria against the Echo-LVH. Pearson correlation and AUC analysis were also performed on single-lead components of ECG-LVH criteria. Results were reported as percentage with their respective 95% confidence interval (CI), and the p < 0.05 was considered statistically significant. Subgroup analyses were performed based on age, body mass index (BMI), and blood pressure. Sensitivity analysis for diagnostic performance was conducted on LVM using a different index, namely height (Palmieri, 1999; Velagaleti et al., 2014). All statistical analysis was carried out in SAS 9.4 (SAS Institute, Cary, NC).

# 3 | RESULTS

# 3.1 | Baseline characteristics and prevalence of LVH

A total of 7415 participants (about 53% female) with an average age of 48 years old and a baseline blood pressure of 126/82 mmHg were finally included in the analysis (Figure 1), among whom 32% were categorized as "hypertension" defined by a seated blood pressure over 140/90 mmHg and 17% were reported to have a history of cardiovascular disease (Table 1). Echo-LVH was detected in 11% of the sample population with an average left ventricular ejection fraction (EF) of 68% and LVMI of 80 g/m<sup>2</sup>. Lower BSA but higher BMI, higher blood pressure and lipid were observed in the Echo-LVH participants. The prevalence of ECG-LVH varied largely, which was 27.3% by Peguero-Lo Presti criteria, 5.3% by Cornell criteria, 3.6% by Cornell product criteria, 10.9% by Sokolow-Lyon criteria, and 3.7% by Sokolow-Lyon product.

# 3.2 | Linear correlation between LVMI and ECG-LVH criteria or its single-lead component

We first treated the calculated ECG-LVH voltage or voltage product as numerical variable and analyzed its correlation with LVMI. As shown in Table 2 and Figure 2, the five ECG-LVH criteria showed relatively weak correlation with Echo-LVH ( $r = .10 \sim 0.21$ , all p < .05), and the highest correlation was observed in Cornell voltage criteria.



**FIGURE 1** The flow chart of participants in the study

To clarify the importance of each component in ECG-LVH criteria, the correlations between LVMI and voltage of R wave or S wave as well as QRS duration in these criteria were also assessed (Table 2).  $R_{aVL}$  showed the highest correlation among all single-lead components (r = 0.18, p < .05), which is consistent with Cornell voltage criteria, namely the sum of  $R_{aVL}$  and  $S_{V3}$ .

# 3.3 | Diagnostic performance of ECG-LVH criteria

We evaluated the diagnostic performance of ECG-LVH criteria when Echo-LVH was taken as reference standard. As presented in Table 3, generally ECG-LVH criteria had low sensitivity, PPV but high specificity and NPV. Peguero-Lo Presti criteria had the best sensitivity (29%, 95%CI: 26%-32%), followed by Cornell voltage (12%, 95% CI: 9%-14%) as well as Sokolow-Lyon voltage (12%, 95% CI: 10%-15%), and finally the Cornell and Sokolow-Lyon product (4%). Peguero-Lo Presti criteria were found to have correspondingly lower specificity (73%, 95% CI: 72%-74%) but even much lower accuracy (68%, 95%CI: 67%-69%), compared with the others. All criteria performed poor with AUC ranged from 0.50 to 0.59, where Cornell duration product had relative better performance (AUC: 0.59, 95% CI: 0.57-0.61). This may be to some extent explained by the single-lead components performance shown in Figure 2, where R<sub>aVL</sub> (AUC: 0.60, 95% CI: 0.58–0.62) and QRS duration (AUC: 0.58, 95% CI: 0.56-0.6) showed a slightly superiority over the rest of single leads.

# 3.4 | Subgroup analysis by age, BMI, and hypertension

Relatively high specificity, low sensitivity, and poor AUC were observed in all subgroups (Figure 3 Figure 2 and Figure S1,S2,S3). As shown in Figure 3 and Figure S1,S2 Peguero-Lo Presti criteria showed the highest sensitivity but lowest specificity and accuracy no matter how our population was stratified by age, hypertension, or BMI. The criteria performed generally better in accuracy and AUC in younger participants, especially those less than 45 years old. Higher sensitivity for these criteria was observed in groups with older age. Moreover, as presented in Figure 3 D-F, ECG criteria had higher sensitivity, lower specificity, and accuracy in subjects with hypertension. Peguero-Lo Presti criteria showed higher AUC in normotensive participants (Figure S2), which is consistent with the larger AUC of deepest S in normotensive ones (Figure S3).

# 4 | DISCUSSION

Here, we obtained the following key findings: 1) All the five ECG-LVH criteria had low sensitivity, PPV but high specificity and NPV. 2) Generally, the five ECG-LVH had weak linear correlation with LVMI and poor discrimination ability with Echo-LVH. 3) Among the five criteria, Peguero-Lo Presti criteria have the highest sensitivity but lowest accuracy and discrimination ability. Cornell voltage product had relatively superior accuracy and AUC but lowest sensitivity. 4) R<sub>aVL</sub> and QRS duration

### TABLE 1 Baseline characteristics of sample population

Characteristics	All (n = 7145)	non-LVH (n = 6580)	Echo-LVH indexed by BSA(n = 835)	P value
Age, y	48.18 ± 14.72	47.13 ± 14.6	56.38 ± 13.03	< 0.0001
Female (%)	3920 (52.87%)	3284 (49.91%)	636 (76.17%)	< 0.0001
BMI, kg/m <sup>2</sup>	24.18 ± 3.57	24.12 ± 3.57	24.69 ± 3.55	< 0.0001
Overweight (%)	2856 (38.52%)	2498 (37.96%)	358 (42.87%)	0.006
BSA	1.69 ± 0.18	$1.7 \pm 0.18$	$1.62 \pm 0.15$	< 0.0001
SBP, mmHg	126.46 ± 19.25	125.33 ± 18.61	135.34 <u>+</u> 21.77	< 0.0001
DBP, mmHg	81.81 ± 10.98	81.55 ± 10.83	83.83 ± 11.9	< 0.0001
Hypertension (%)	2397 (32.46%)	1999 (30.49%)	398 (48.07%)	< 0.0001
total cholesterol(mmol/l)	4.93 ± 1.1	4.91 ± 1.1	5.06 ± 1.11	0.0005
TG (mmol/l)	1.37 (0.94, 2.01)	1.35 (0.93, 2)	1.52 (0.99, 2.14)	< 0.0001
Serum Creatine(umol/l)	67.42 ± 23.29	67.69 ± 17.34	$65.31 \pm 48.62$	0.008
Smoking (%)	1855 (25.44%)	1722 (26.57%)	133 (16.42%)	< 0.0001
Drinking (%)	1491 (20.48%)	1397 (21.59%)	94 (11.62%)	< 0.0001
Past history of cardiovascular disease (%)	1222 (16.66%)	959 (14.73%)	263 (31.88%)	<0.0001

Abbreviations: BMI = body mass index; DBP = diastolic blood pressure; LVM = left ventricular mass; LVMI = left ventricular mass index; SBP: systolic blood pressure; TG = triglycerides.

Note: Data are presented as mean ± standard deviation or n (%)

 TABLE 2
 Linear correlation between LVMI and ECG-LVH criteria

 or its single-lead component
 Item (Component)

Variable	Correlation	P value
ECG Criteria		
Peguero-Lo Presti	0.14	<0.0001
Gender-specific Cornell voltage	0.21	<0.0001
Cornell voltage product	0.14	<0.0001
Sokolow-Lyon voltage	0.15	<0.0001
Sokolow-Lyon voltage product	0.16	<0.0001
ECG criteria components		
R <sub>aVL</sub>	0.18	<0.0001
R <sub>V5</sub>	0.16	<0.0001
R <sub>V6</sub>	0.11	<0.0001
S <sub>V1</sub>	0.06	0.6108
S <sub>V3</sub>	0.14	<0.0001
S <sub>V4</sub>	0.13	<0.0001
deepest S	0.12	0.0092
QRS duration	0.08	0.6552

had stronger association with Echo-LVH compared with other singlelead components 5) Hypertensive and older individuals had higher sensitivity but lower specificity and accuracy than their counterparts.

# 4.1 | Prevalence of Echo-LVH in a Chinese general population

We reported that the prevalence of Echo-LVH determined by BSAindexed LVM accounted for 11% in the Chinese general population,

a slightly lower value than found in previous studies describing the prevalence of LVH being from 13% to 20% (Gallego et al., 2009; Xu et al., 2015; Stewart et al., 2018). This may be due to different population or racial differences in progression of LVH (Weber, 1991). Methodological issues like index approaches may be another interpretation. The rate of Echo-LVH defined by height (Palmieri et al., 1999; Velagaleti et al., 2014). indexed LVM was much higher compared with that of Echo-LVH indexed by BSA (24% vs.11%) in our population, which suggested that different thresholds for abnormality are critical and need further investigation. Whether echo LVH indexed by height or BSA reflects LVH more accurately is a guestion that MRI or more advanced techniques may be required to answer. Limited studies have so far referred to this issue. Differences in baselines between Echo-LVH and non-Echo-LVH suggested that in individuals with risk factors of aging, female, hypertension, and obesity, an early screening of LVH by electrocardiology or echocardiography is needed.

# 4.2 | Association between Echo-LVH and ECG-LVH

Our study found all the main ECG-LVH criteria had low sensitivity and PPV as well as high specificity and NPV. The PPV ranges from 12 to 24% while NPV was around 89%. We also assessed the diagnostic performance of Romhilt-Estes score, another ECG criterion that involves T wave abnormalities, abnormal voltages in limb leads and a widened QRS duration (Romhilt & Estes, 1968). Low sensitivity (2%), low PPV (21%), high specificity (99%), and high NPV (89%) were again observed, which suggested Romhilt-Estes score may be more useful for excluding the presence of LVH in our population. The high NPV of ECG-LVH suggested we would be more confident to rule out Echo-LVH with a normal voltage (or voltage product) in ECG. Discrepancies



FIGURE 2 Area under the ROC Curve (AUC) and correlation between the main ECG-LVH criteria or single lead and Echo-LVH. BSA indexed LVM (LVMI) was applied for determination of Echo-LVH. AUC and 95% confidence interval (95% CI), as well as correlation, were presented to evaluate the discrimination ability of ECG-LVH criteria to identify Echo-LVH

TABLE 3 Diagnostic statistics of ECG-LVH criteria for Echo-LVH

ECG criteria	Sensitivity(95%CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy(95%CI)
Peguero-Lo Presti	29(26, 32) <sup>*</sup>	73(72, 74)*	12(11, 14)	89(88, 90)	68(67, 69)
Cornell voltage	12(9, 14)*	95(95, 96) <sup>*</sup>	24(20, 29)*	89(89, 90)	86(85, 87)
Cornell product	4(3, 5) <sup>*</sup>	96(96, 97) <sup>*</sup>	12(8, 16)	89(88, 90)	86(85, 87)
Sokolow-Lyon voltage	12(10, 15) <sup>*</sup>	89(89, 90) <sup>*</sup>	13(10, 15)	89(88, 90)	81(80, 82)
Sokolow-Lyon product	4(3, 6) <sup>*</sup>	96(96, 97) <sup>*</sup>	13(9, 17)	89(88, 90)	86(85, 87)
Sokolow-Lyon Voltage Sokolow-Lyon product	4(3, 6) <sup>*</sup>	96(96, 97) <sup>*</sup>	13(10, 15)	89(88, 90) 89(88, 90)	86(85, 87)

ECG-LVH, electrocardiographic left ventricular hypertrophy. PPV: positive predictive values. NPV: negative predictive values

Accuracy was defined as the percentage of correctly classified instances (True Positive Rate + True Negative Rate)/(True Positive Rate + True Negative Rate + False Positive Rate + False Negative Rate)

\*p < .05: P value stands for pair-wise comparison of sensitivity, specificity, PPV, NPV or accuracy between ECG criteria using Fisher's Exact test, where Peguero-Lo Presti taken as the reference.

between ECG criteria to detect Echo-LVH were noticed. Previous studies reported a higher specificity in Cornell and a higher sensitivity in Sokolow-Lyon criteria (Truong et al., 2016), the two ECG-LVH criteria most commonly used in practice. Cornell voltage showed higher correlation and diagnostic performance compared Sokolow-Lyon criteria for LVMI (Fang et al., 2017; Xu et al., 2015). Recently, the newer Peguero-Lo Presti criterion defined by the sum of the deepest S wave and S wave in lead V4 has been validated as one of the best criteria by AUC analysis theoretically based on the change of cardiac depolarization vector (Peguero et al., 2017). However, Sun et al found it was inferior to Cornell criterion in a Chinese population from Liaoning province (Sun et al., 2018). Here, we obtained the similar results that the diagnostic performance of Cornell voltage was better than Sokolow-Lyon and Peguero-Lo Presti criteria, though Peguero-Lo Presti criteria had the highest sensitivity among aforementioned five ECG criteria. Additionally, we found Cornell voltage

product even had slightly better diagnostic performance than Cornell voltage. Further AUC analysis of single-lead component demonstrated a greater importance of R wave voltage than S wave alone in the diagnosis of Echo-LVH in Chinese population. These inconsistent results from different population may be explained by ethnicity, sample population, and enrollment of participants, as aforementioned in previous studies (Peter et al., 2017; Sun et al., 2018). Despite of the numerous ECG-LVH criteria, it is warranted to explore better screening method for different regional population (Narita et al., 2019).

# 4.3 | Association between Echo-LVH and singlelead component for ECG-LVH

ECG-LVH criteria were different combinations of multiple components. Here, we found QRS duration and  $R_{aVL}$  had stronger



FIGURE 3 The sensitivity, specificity, and accuracy of the five ECG criteria stratified by age and hypertension

association with Echo-LVH among all other single-lead components, which may drive the better performances of Cornell-related and product-related criteria. QRS duration was reported to be an independent predictor for LVH in previous studies (Okin et al., 2002; Palmieri et al., 2007). Potential mechanisms included the longer time required to activate myocardium that was increasingly distant from specialized conduction tissue and the decreased conduction velocity in hypertrophied myocardium. In addition, products of voltage and duration may have a more accurate approximation of time-voltage integral of QRS complex, which has been associated with LVH (Okin et al., 1995; Palmieri et al., 2007). This may explain the stronger association between Echo-LVH and the two "product" criteria, namely Sokolow-Lyon and Cornell product criteria, compared with the one using voltage alone.  $R_{aVI}$ was also a good and reproducible index for LVH. Some studies even suggested it as the first line to detect LVH (Courand et al., 2015;

Gosse et al., 2012). This may because  $R_{aVL}$  reflects most of vectors, directed leftward and superiorly, originating from activation of the left ventricle (Verdecchia et al.,2009).

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# 4.4 | Subgroup analysis stratified by age and hypertension

Older age, hypertension, and obesity are risk factors of processing LVH (Aj & Gr, 2015; Shao et al., 2019; Cheng et al., 2010; Turkbey et al., 2010). We observed that hypertensive and older individuals had higher sensitivity but lower specificity and accuracy than their counterparts. Echo-LVH was reported to be more prevalent in hypertensive and older individuals, which may contribute to the higher sensitivity in these populations. The decrease of accuracy indicates the drop of specificity, and the 11% prevalence of Echo-LVH had

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more predominant effects than the increase of sensitivity in hypertensive and older population. Taking all these results into consideration, differences in ECG-LVH by age and blood pressure might suggest specific criteria for hypertensive population and age-specific criteria in addition to the factor of sex.

# 4.5 | Discrepancy between ECG-LVH and LVH by imaging

We noticed weak linear correlations between ECG-LVH and LVMI as well as poor discriminative ability of ECG-LVH to detect Echo-LVH. We speculate that the role of Echo-LVH, or even the current gold standard MRI-LVH, as a reference standard to be compared with ECG-LVH may need to be re-examined. The interpretation of the association between ECG and imaging should be cautious: instead of just regarding them as equivalent approaches for LVH detection and taking one as reference standard to validate another, potential distinction of the true nature between these two approaches may be reconsidered. In theory, ECG reflects the electrical signal of the whole heart while imaging predicts the cardiac structure and function. Different evaluation may reveal different functionalities, either diagnosis or prediction (Bacharova, 2009; Li et al., 2014; Narayanan et al., 2014). It has been reported that ECG-LVH can predict the outcome of heart failure, outperforming MRI-LVH (Oseni et al., 2017). Further study is warranted for the comparisons between individuals with isolated ECG-LVH, imaging-LVH or both of these two, as well as pathophysiological mechanisms behind these two approaches.

# 5 | LIMITATIONS

Firstly, we used Echo-LVH as reference standard rather than MRI. However, LVH estimated by 2D-echocardiography is still the most widely used method in clinical practice. Secondly, we did not analyze the association between ECG-LVH and Echo-LVH in multi-variate model. However, we still considered both ECG-LVH and Echo-LVH as diagnostic criteria to detect LVH. Thus, covariate variables were not adjusted.

# 6 | CONCLUSION

In the present study, we assessed the association between major ECG-LVH criteria and LVH diagnosed by echocardiology in a Chinese general population. ECG-LVH criteria had high negative predictive value to detect Echo-LVH. Though with higher sensitivity, Peguero-Lo Presti criteria did not have better diagnostic performance than traditional ECG-LVH criteria to detect Echo-LVH.  $R_{aVL}$  and QRS duration had stronger association with Echo-LVH among all single-lead components.

# 7 | AFFILIATIONS

Department of Cardiology, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University; Department of Cardiology, Peking University People's Hospital; Peking University Clinical Research Institute; Jining NO. 1 People's Hospital; The First Hospital of China Medical University; Shanxi Academy of medical sciences, Shanxi Dayi Hospital; The First hospital of Lanzhou University; The Second Affiliated Hospital of Nanchang University; The Affiliated Hospital of Guiyang Medical College; Department of Cardiology, the First Affiliated Hospital of Shantou University Medical College; Xuzhou Central Hospital; Beijing First Hospital of Integrated Chinese and Western Medicine.

# 8 | DEVELOPMENT

Jing Yang, Guijin Wang, Lingyun Kong, Hua Li, Xingjie Li, Yingxian Sun, Xuewen Li, Zheng Zhang, Xiaoshu Cheng, Lirong Wu, Xuerui Tan, Bing Han, Jiayu Wang, and Zhaoguo Zhang performed

# 9 | ACQUISITION OF DATA

Tingting Lv and Yifang Yuan drafted and designed of the manuscript.

Yifang Yuan, Tingting Lv, and Huijuan Li statistical analyzed the study.

Ping Zhang performed study site supervision and manuscript revisions.

### 10 | What Is New?

We analyzed the association between main ECG-LVH criteria, including a recently reported criterion, and Echo-LVH in a general Chinese population. The performance of each single-lead component was also evaluated.

# 11 | What Are the Clinical Implications?

We confirmed the negative predictive value of ECG as a routine screening tool to rule out Echo-LVH. The performance of the recently reported Peguero-Lo Presti criteria questioned its generalizability in Chinese population. The better performance of  $R_{aVL}$  and QRS duration among all single-lead components supports their potential application in the development of future ECG-LVH criteria.

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### AUTHOR CONTRIBUTIONS

Ping Zhang had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Ping Zhang, Jihong Guo, Yangfeng Wu, and Yanfang Wang involved in study concept.

# ORCID

Ping Zhang () https://orcid.org/0000-0002-5843-1108

# REFERENCES

- Aj, W., & Gr, N. (2015). Obesity and left ventricular hypertrophy: the hypertension connection. Current Hypertension Reports, 17(4), 539
- Bacharova, L. (2009). Electrocardiography–left ventricular mass discrepancies in left ventricular hypertrophy: electrocardiography imperfection or beyond perfection? *Journal of Electrocardiology*, 42(6), 593–596
- Bauml, M. A., & Underwood, D. A. (2010). Left ventricular hypertrophy: an overlooked cardiovascular risk factor. *Cleveland Clinic Journal of Medicine*, 77(6), 381–387
- Casale, P. N., Devereux, R. B., Alonso, D. R., Campo, E., & Kligfield, P. (1987). Improved sex-specific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: validation with autopsy findings. *Circulation*, 75(3), 565–572. https://doi.org/10.1161/01.CIR.75.3.565
- Casale, P. N., Devereux, R. B., Kligfield, P., Eisenberg, R. R., Miller, D. H., Chaudhary, B. S., & Phillips, M. C. (1985). Electrocardiographic detection of left ventricular hypertrophy: development and prospective validation of improved criteria. *Journal of the American College* of Cardiology, 6(3), 572–580
- Chapman, J. N., Mayet, J., Chang, C. L., Foale, R. A., Thom, S. A., Poulter, N. R. (1999). Ethnic differences in the identification of left ventricular hypertrophy in the hypertensive patient. *American Journal of Hypertension*, 12(5), 437–442
- Cheng, S., Xanthakis, V., Sullivan, L. M., Lieb, W., Massaro, J., Aragam, J., Benjamin, E. J., & Vasan, R. S. (2010). Correlates of echocardiographic indices of cardiac remodeling over the adult life course: longitudinal observations from the Framingham Heart Study. *Circulation*, 122(6), 570–578
- Courand, P. Y., Grandjean, A., Charles, P. et al (2015). R Wave in aVL Lead is a Robust Index of Left Ventricular Hypertrophy: A Cardiac MRI Study. American Journal of Hypertension, 28(8), 1038–1048
- Devereux, R. B., Alonso, D. R., Lutas, E. M., Gottlieb, G. J., Campo, E., Sachs, I., & Reichek, N. (1986). Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. *The American Journal of Cardiology*, *57*(6), 450–458
- Drazner, M. H., Rame, J. E., Marino, E. K., Gottdiener, J. S., Kitzman, D. W., Gardin, J. M., Manolio, T. A., Dries, D. L., & Siscovick, D. S. (2004). Increased left ventricular mass is a risk factor for the development of a depressed left ventricular ejection fraction within five years: the Cardiovascular Health Study. *Journal of the American College of Cardiology*, 43(12), 2207–2215
- Fang-Ying, S., Yi-Hwei, L., Yen-Po, L., Chung-Jen, L., Chih-Hung, W., Fan-Chun, M., Yun-Shun, Y., Felicia, L., Hsien-Tsai, W., Gen-Min, L. (2017). A comparison of Cornell and Sokolow-Lyon electrocardiographic criteria for left ventricular hypertrophy in a military male population in Taiwan: the Cardiorespiratory fitness and HospItalization Events in armed Forces study. *Cardiovasc Diagn Ther*, 7(3), 244–251

- Gallego-Delgado, J., Connolly, S. B., Lázaro, A., Sadlier, D., Kieran, N. E., Sugrue, D. D., Doran, P., Brady, H. R., Osende, J., & Egido, J. (2009).
   Transcriptome of hypertension-induced left ventricular hypertrophy and its regression by antihypertensive therapies. *Hypertension Research*, 32(5), 347–357
- Gosse, P., Jan, E., Coulon, P., Cremer, A., Papaioannou, G., & Yeim, S. (2012). ECG detection of left ventricular hypertrophy: the simpler, the better? *Journal of Hypertension*, 30(5), 990–996. https://doi. org/10.1097/HJH.0b013e3283524961
- Hancock, E. W., Deal, B. J., Mirvis, D. M., Okin, P., Kligfield, P., Gettes, L. S., Bailey, J. J., Childers, R., Gorgels, A., Josephson, M., Kors, J. A., Macfarlane, P., Mason, J. W., Pahlm, O., Rautaharju, P. M., Surawicz, B., van Herpen, G., Wagner, G. S., Wellens, H. (2009). AHA/ACCF/ HRS recommendations for the standardization and interpretation of the electrocardiogram: part V: electrocardiogram changes associated with cardiac chamber hypertrophy: 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. *Journal of the American College of Cardiology*, 53(11), 992–1002
- Jain, A., Tandri, H., Dalal, D. et al (2010). Diagnostic and Prognostic Utility of ECG for Left Ventricular Hypertrophy Defined by MRI in Relationship to Ethnicity: The Multi-Ethnic Study of Atherosclerosis (MESA). American Heart Journal, 159(4), 652–658.
- Khaled, A., Kevin, W., Tim, J., John, R., Alistair, S. H., Mohan, S. (2004) New gender-specific partition values for ECG criteria of left ventricular hypertrophy: recalibration against cardiac MRI. *Hypertension*, 44(2), 175–179
- Lang R. M., Badano L. P., Mor-Avi V., Afilalo J., Armstrong A., Ernande L., Flachskampf F. A., Foster E., Goldstein S. A., Kuznetsova T., Lancellotti P., Muraru D., Picard M. H., Rietzschel E. R., Rudski L., Spencer K. T., Tsang W., & Voigt J.-U. (2015). Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. European Heart Journal - Cardiovascular Imaging, 16(3), 233–271. http://dx.doi. org/10.1093/ehjci/jev014
- Li, H., Pei, F., Shao, L., Chen, J., Sun, K., Zhang, X., Zhang, C., Liu, J., Xiao, C., & Hui, R. (2014). Prevalence and risk factors of abnormal left ventricular geometrical patterns in untreated hypertensive patients. BMC Cardiovascular Disorders, 14(1), https://doi. org/10.1186/1471-2261-14-136
- Molloy, T. J., Okin, P. M., Devereux, R. B., & Kligfield, P. (1992). Electrocardiographic detection of left ventricular hypertrophy by the simple QRS voltage-duration product. *Journal of the American College of Cardiology*, 20(5), 1180–1186
- Narayanan, K., Reinier, K., Teodorescu, C., Uy-Evanado, A., Chugh, H., Gunson, K., Jui, J., & Chugh, S. S. (2014). Electrocardiographic versus echocardiographic left ventricular hypertrophy and sudden cardiac arrest in the community. *Heart Rhythm: the Official Journal of the Heart Rhythm Society*, 11(6), 1040–1046
- Narita, M., Yamada, M., Tsushima, M., Kudo, N., Kato, T., Yokono, Y., Toyama, Y., Senoo, M., Yonekura, M., Narita, N., Kimura, Y., Sawada, K., Tokuda, I., & Tomita, H. (2019). Novel Electrocardiographic Criteria for the Diagnosis of Left Ventricular Hypertrophy in the Japanese General Population. *International Heart Journal*, 60(3), 679–687
- Okin, P. M., Jackson T. W., Markku S. N., Sverker J., Anne L. T., Robert P., Vasilio P., Luther T. C., Elizabeth O. O., Otelio S. R., Lasse O., Matti V., Lauri T., Stevo J., Björn D., Richard B. D. (2002). Ethnic differences in electrocardiographic criteria for left ventricular hypertrophy: the LIFE study. Losartan Intervention for Endpoint. American Journal of Hypertension, 15(8), 663–671

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- Okin, P. M., Roman, M. J., Devereux, R. B., & Kligfield, P. (1995). Electrocardiographic identification of increased left ventricular mass by simple voltage-duration products. *Journal of the American College of Cardiology*, *25*(2), 417-423
- Oseni, A. O., Qureshi, W. T., Almahmoud, M. F. et al (2017). Left ventricular hypertrophy by ECG versus cardiac MRI as a predictor for heart failure. *Heart*, 103(1), 49–54
- Palmieri, V., Dahlöf, B., DeQuattro, V., Sharpe, N., Bella, J. N., de Simone, G., Paranicas, M., Fishman, D., Devereux, R. B. (1999). Reliability of echocardiographic assessment of left ventricular structure and function: the PRESERVE study. Prospective Randomized Study Evaluating Regression of Ventricular Enlargement. *Journal of the American College of Cardiology*, 34(5), 1625–1632
- Palmieri, V., Okin, P. M., de Simone, G. et al (2007). Electrocardiographic characteristics and metabolic risk factors associated with inappropriately high left ventricular mass in patients with electrocardiographic left ventricular hypertrophy: the LIFE Study. Journal of Hypertension, 25(5), 1079–1085
- Peguero, J. G., Lo Presti, S., Perez, J., Issa, O., Brenes, J. C., & Tolentino, A. (2017). Electrocardiographic Criteria for the Diagnosis of Left Ventricular Hypertrophy. *Journal of the American College of Cardiology*, 69(13), 1694
- Romhilt, D., & Estes, E. (1968). A point-score system for the ECG diagnosis of left ventricular hypertrophy. *American Heart Journal*, 75(6), 752–758. https://doi.org/10.1016/0002-8703(68)90035-5.
- Shao, Q., Meng, L., Tse, G., Sawant, A. C., Zhuo Yi Chan, C., Bazoukis, G., Baranchuk, A., Li, G., & Liu, T. (2019). Newly proposed electrocardiographic criteria for the diagnosis of left ventricular hypertrophy in a Chinese population. *Annals of Noninvasive Electrocardiology*, 24(2), e12602. https://doi.org/10.1111/anec.12602
- Sokolow, M., & Lyon, T. P. (1949). The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. *American Heart Journal*, 37(2), 161–186
- Stewart, S., Lavie, C. J., Shah, S., Englert, J., Gilliland, Y., Qamruddin, S., Dinshaw, H., Cash, M., Ventura, H., & Milani, R. (2018). Prognostic Implications of Left Ventricular Hypertrophy. Progress in Cardiovascular Diseases 61(5-6), 446–455
- Sun, G. Z., Wang, H. Y., Ye, N., & Sun, Y. X. (2018). Assessment of novel Peguero-Lo Presti electrocardiographic left ventricular hypertrophy criteria in a large Asian population: Newer may not be better. *Canadian Journal of Cardiology*, 34(9), 1153–1157. https://doi. org/10.1016/j.cjca.2018.05.013
- Truong, Q. A., Ptaszek, L. M., Charipar, E. M., Taylor, C., Fontes, J. D., Kriegel, M., Irlbeck, T., Toepker, M., Schlett, C. L., Bamberg, F., Blankstein, R., Brady, T. J., Nagurney, J. T., & Hoffmann, U. (2010). Performance of electrocardiographic criteria for left ventricular hypertrophy as compared with cardiac computed tomography: from the Rule Out Myocardial Infarction Using Computer Assisted Tomography trial. *Journal of Hypertension*, 28(9), 1959–1967

- Turkbey, E. B., McClelland, R. L., Kronmal, R. A. et al (2010). The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). JACC: Cardiovascular Imaging, 3(3), 266-274
- Velagaleti, R. S., Gona, P., Pencina, M. J., Aragam, J., Wang, T. J., Levy, D., D'Agostino, R. B., Lee, D. S., Kannel, W. B., Benjamin, E. J., & Vasan, R. S. (2014). Left ventricular hypertrophy patterns and incidence of heart failure with preserved versus reduced ejection fraction. *The American Journal of Cardiology*, 113(1), 117–122 https://doi. org/10.1016/j.amjcard.2013.09.028.
- Verdecchia, P., Angeli, F., Cavallini C., Mazzotta, G., Repaci, S., Pede, S., Borgioni, C., Gentile, G., Reboldi, G. (2009). The voltage of R wave in lead aVL improves risk stratification in hypertensive patients without ECG left ventricular hypertrophy. *Journal of Hypertension*, 27(8), 1697–1704
- Weber, J. R. (1991). Left ventricular hypertrophy: Its prevalence, etiology, and significance. *Clinical Cardiology*, 14(S3), 13–17
- Xu, C. F., Tan, ESJ, Feng, L., Santhanakrishnan, R., Chan, MMY, Nyunt, S.
   Z., Ng, T. P., Ling, L. H., Richards, A. M., Lam, CSP, Lim, T. W. (2015).
   Electrocardiographic Criteria for Left Ventricular Hypertrophy in Asians Differs from Criteria Derived from Western Populations-Community-based Data from an Asian Population. Annals of the Academy of Medicine, Singapore, 44(8), 274–283.
- Zile, M. R., Gottdiener, J. S., Hetzel, S. J., McMurray, J. J., Komajda, M., McKelvie, R., Baicu, C. F., Massie, B. M., & Carson, P. E. (2011). Prevalence and significance of alterations in cardiac structure and function in patients with heart failure and a preserved ejection fraction. *Circulation*, 124(23), 2491–2501 https://doi.org/10.1161/ CIRCULATIONAHA.110.011031

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