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Full Length Research Paper

Better criterion screening for left ventricular hypertrophy by electrocardiogram with different purposes

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According to the recommendations for the standardization and interpretation of the electrocardiogram (ECC) of AHA/ACCF/HRS declared in 2009, there are more than 30 criteria for diagnosing left ventricular hypertrophy (LVH). The sensitivity of the various criteria is generally quite low. However, the specificity of ECG in LVH could be 85 to 90%, acting as a strong predictor for cardiovascular events. To investigate the proper criteria in epidemiological screening with different purpose, 5209 qualified ECG out of 6830 people were selected from cross-sectional Handan eye study. Two criteria were chosen: (1) Sokolow-Lyon index, sum of SV1+RV5 or V6 35 mm; (2) Cornell voltage duration product, men: (SV3+RaVL)×QRS duration 2440 ms; women: (SV3+(RaVL+8 mV))×QRS duration 2440 ms. The ECG-LVH group contains 829 individuals (12.18% of the cohort), including 607 by Sokolow-Lyon index and 278 by Cornell voltage duration product. After data estimation, we found that there were no statistical differences between ECG-LVH population and normal population. While evaluated these data in the group that have retinopathy without diabetes, the Sokolow- Lyon index and Cornell voltage duration product were statistically different with normal population (P= 0.023 and P= 0.014, respectively). We use the simple MiniMental State Examination (MMSE) to evaluated the mental status of the population and found that when the score was above 15, there was no statistically different between the positive and negative people in Sokolow-Lyon index (P= 0.135); however, in evaluated Cornell voltage duration product, there was statistical difference (P=0.001). When we evaluated the data associated with atherosclerotic factors, we found no differences in Cornell voltage-duration product; as for the Sokolow -Lyon index, the differences were shown in systolic blood pressure, total cholesterols and uric acid (P= 0.03, 0.04 and 0.04, respectively). Different criterion should be chosen for different purposes. For atherosclerotic screening or epidemiological survey of cardiovascular diseases, the Sokolow-Lyon index might be better. If we use the criterion for epidemiological ophthalmology such as our Handan eye study, both Sokolow-Lyon index and Cornell voltage duration product could be used. As for the evaluation of mental status and its relationship with the LVH risk factors, we might choose Cornell voltage duration product.

Key words: Left ventricular hypertrophy, electrocardiagram, Sokolow-L(l)yon index, Cornell voltage-duration product.

INTRODUCTION

Hypertension is a major cause of coronary heart disease, stroke and heart failure. Several studies have shown that, left ventricular hypertrophy (LVH) is an important risk factor in patients with hypertension, leading to a 5-fold to 10-fold increase in cardiovascular risk, (Kannel et al., 1969, 1970; Haider et al., 1998; Verdecchia et al., 1998; Sundström et al., 2001) which is similar to the increase

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seen in patients with a history of myocardial infarction (Dunn et al., 1990). Left ventricular hypertrophy is considered as the target organ damage (TOD) in the heart. The latest idea has considered it as a complicated clinical syndrome far more beyond merely TOD. The mechanism of LVH remains unclear. Accurate and early diagnosis of left ventricular hypertrophy is therefore, an important component for the care of patients with hypertension. Decisions about treatment should be based on assess-ments of hypertensive target organ damage and overall cardiovascular risk. As the main diagnostic method and one of the 4 basic health-screening items, electrocardio-gram plays an important role in LVH diagnoses. According to the new2009 recommendations for the standardization and interpretation of the electrocardiogram of AHA/ ACCF/HRS, this economic method has been valued not only for clinical diagnosis, but also for epidemiological evaluation (Hancock et al., 2009). The specificity of ECG in LVH could be 85 to 90%. On the other hand, ECG is considered as the second-line diagnosing method according to its low sensitivity. The 2009 recommenda-tions for the standardization and interpretation of the electrocardiogram of AHA/ACCF/HRS, part V: electro-cardiogram changes associated with cardiac chamber hypertrophy mentioned more than 30 criteria for diagnosing LVH. The sensitivity of the various criteria is generally quite low (usually less than 50%). However, the sensitivity and specificity of each criterion is different. Thus, the diagnostic accuracy will depend on the specific criterion used (Hancock et al., 2009).

POPULATION

We choose ECG to diagnosis left ventricular hypertrophy with our analysis for Handan Eye Study. The Handan eye study (HES) was designed to determine the prevalence and impact of eye diseases among rural populations in China. The study was funded by the China Ministry of Science and Technology, China Ministry of Health and Handan City Bureau of Science and Technology, Yongnian County, Handan, located in the south part of Hebei province (about 500 km south of Beijing) has demographic characteristics similar to other rural Chinese locations according to the 2000 National Census (Wang et al., 2009). The HES is a population-based cohort study in a rural population in northern China conducted in 2006 and 2007. Full details of the methods have been described previously. In brief, 7557 eligible people of Yongnian County, Handan, Hebei province, aged 30 years were identified from 13 randomly selected villages using a stratified, clustered and multistaged sampling technique with probabilities proportionate to the size of population in each cluster. We examined the prevalence and impact of eye diseases in non-institutionalized, community dwelling persons aged 30 years or older in Yongnian County, Handan City, to determine both modifiable and non-modifiable risk factors that may be associated with ocular diseases and to understand the barriers to use of eye care services in this region. Ethics committee approval was obtained from the Beijing Tongren Hospital review board and written informed consent was obtained from all subjects, those who cannot read or write were asked to stamp with right forefinger (Liang et al., 2009).

METHODS

We selected 5209 qualified ECG from these 6830 people. Each ECG has complete information for LVH analyses. As to the new recommendation of standardization in 2009, the LIFE study and previous systemic review mentioned in BMJ, we choose 2 criteria: (1) Sokolow-Lyon index (Sokolow and Lyon, 1949), sum of SV1+RV5 or V6 35 mm; (2) Cornell voltage duration product (Molloy et al., 1992) men: (SV3+RaVL)xQRS duration 2440 ms; women: (SV3+(RaVL+8 mV))xQRS duration 2440 ms.

Based on these criteria, we screened 2519 hypertensive patients with the JNC7 criteria of high blood pressure (systolic pressure 140 mmHg and/or diastolic pressure 90 mmHg). The ratio of the whole population examined was 45.10%, merely more than the standardized ratio of Hebei Province in the report on cardiovascular diseases in China, 2007 (41.05%) (Peng et al., 2010). The ECG-LVH group contains 829 (12.18% of the cohort), including 607 by Sokolow-Lyon index and 278 by Cornell voltage duration product. LVH patients with hypertension are 580 (23.03% of hypertensive patients, 69.96% of ECG- LVH population). The screening was described as in Figure 1. The central clinical examination was shown as follows:

Central clinic examination of HES

Questionnaires

Subjects were interviewed by trained staff about demographic information, quality of life (EuroQol-5D, VF/QoL), (Zhao et al., 1998; Espallargues et al., 2005; Langelaan et al., 2007) and cognitive status (the MiniMental State Examination, MMSE) (West et al., 2003), as well as medical conditions, family history of eye diseases and barriers for seeking eye care.

Physical examination

Height, weight, waist-hip circumference, pulse rate and blood pressure were measured according to a standardized protocol by certified nurses (Foong et al., 2007).

Measurements of physical function

Electrocardiogram was obtained on all who attended the central clinic. Ankle- brachial index, toe-brachial index and pulse wave velocity were measured with a Colin BP-203RPE II (VP-1000) (Colin, Komaki, Japan). Physical mobility testing was also measured according to protocol (Guralnik et al., 1994; Friedman et al., 2007).

Blood collection

Every subject was requested to fast for at least 8 h prior to blood drawing and this was facilitated by collecting blood in the villages between 7:00 and 9:00 a.m. Sterile vacuum tubes with and without ethylenediaminetetraacetic acid (EDTA) was used and

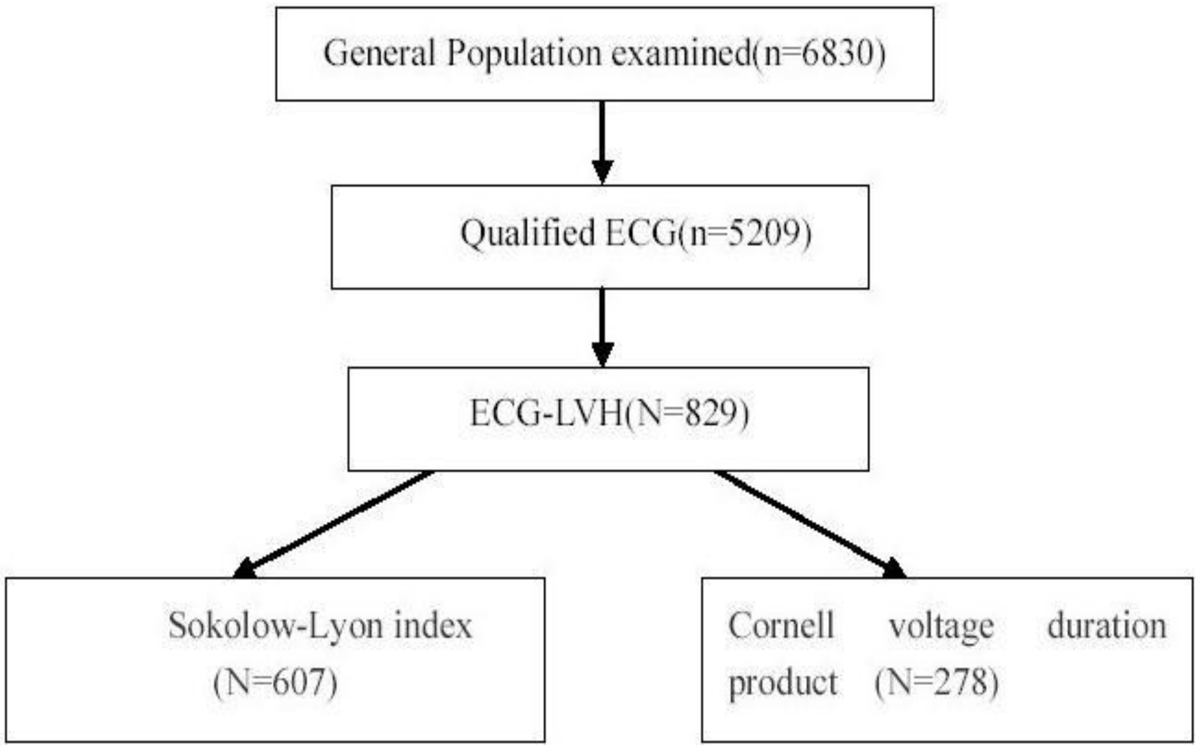

Figure 1. Flowchart for ascertainment in ECG-LVH in the Handan eye study Cohort.

centrifugation was done in the village soon after blood collection. Serum was analyzed for (1) lipids: total cholesterol, total triglycerides, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol; (2) serum creatinine; (3) blood urea nitrogen; (4) fasting glucose in the laboratory of Handan central hospital (the quality control in the laboratory was certified and monitored yearly by Ministry of Health, China).

Urine collection

Urine was collected at the same time of blood drawing into a clean plastic cup and brought back to the laboratory of Handan central hospital for analysis.

Statistical analysis

Statistical analysis was performed by using standard statistical software (SAS9.1.3 and SPSS13.0) . Differences in prevalence between age groups and gender were analyzed by using chi-square test. Frequency of the risk factor in people was compared using chi-square tests. We performed multiple logistic regressions to control for effects of age, gender, and other potential confounders. For continuous traits, t-tests, analysis of variance (ANOVA), analysis of covariance (ANCOVA) and linear regression models were used.

RESULTS

We estimated data among ECG-LVH population and found no statistical differences with normal population. When these data were evaluated in detail, we found that, in the group that have retinopathy without diabetes, the Sokolow-Lyon index and Cornell voltage duration product are statistically different with normal population (Table 1).

The life quality questionnaire includes the evaluation on mobility, self-care, daily activities, pain/discomfort, the illness affecting oneself, relatives or someone needing you care. The evaluations show that the scores on different levels have no statistically different when Sokolow-Lyon index or Cornell voltage duration product are evaluated.

We used the simple MMSE to evaluate the mental status of the populations and found that when the score is above 15, there is no statistically different between the positive and negative groups in Sokolow-Lyon index; however, while evaluating the Cornell voltage duration product, there is statistically difference (Table 2).

When we evaluated the data associated with atherosclerotic factors, we found no differences in Cornell voltage-duration product; as for the Sokolow-Lyon index, the differences were shown in systolic blood pressure, total cholesterols and uric acid. The details are shown in the Table 3.

DISCUSSION

The prevalence of LVH in hypertension is different when the methodology is different. The main methods for diagnosing LVH are electrocardiogram (ECG),

Table 1. LVH Indexes in retinopathy without diabetes and normal population.

Indexes	Retinopathy without diabetes (n= 511)	Normal population (n= 4644)	P
Sokolow-Lyon index	26.11±7.09	25.30±7.51	0.023*
Cornell voltage duration product	1557.1±620.81	1491.4±568.09	0.014*

*, P < 0.05.

Table 2. LVH indexes in MMSE evaluation (N= 2966).

Indexes	MMSE 15 (n= 743)	MMSE<15 (n= 2223)	P
Sokolow-Lyon index	25.34±7.62	25.93±7.63	0.135
Cornell voltage duration product	1520.4±586.96	1442.8±539.31	0.001*

*, P < 0.05.

echocardiology (UCG) and magnetic resonance imaging (MRI). 3D -UCG and MRI have high specificity and sensitivity, with high expenses and immaneuverability. Therefore, 2D-UCG and ECG have been used more in clinical and epidemiological evaluations. Since ECG has been used more than a century, the follow-up investigation is well established and the evidences are persuasive.

ECG is an available and economic method and still be used as the routine clinical item in disease screening. It is still used wildly in epidemiological researches. The appropriate diagnostic work- up of suspected left ventricular hypertrophy in patients with hypertension is less clear; however, different electrocardiographic indexes for the diagnosis of left ventricular hypertrophy, based on the standard 12 lead electrocardiogram, have been described. Many of the proposed indexes have remained anecdotal, but others are commonly used, including the Sokolow-Lyon index, (Sokolow and Lyon, 1949), the Cornell voltage index, (Casale et al., 1985) the Cornell product index, (Norman and Levy, 1996), the Gubner index (Gubner and Ungerleider, 1943) and the Romhilt-Estes scores (Romhilt and Estes, 1968). However, debate about their comparative diagnostic value continues (Schillaci et al., 1998; Verdecchia et al., 2000; Conway and Lip, 2001).

Pewsner et al. (2007) did a systematic review to clarify the accuracy of different electrocardiographic indexes, with emphasis on their ability to rule out left ventricular hypertrophy in patients with arterial hypertension. 21 studies and data on 5608 patients were analyzed. This systematic review of studies of the accuracy of diagnostic tests found that the accuracy of electrocardiographic indexes in the diagnosis of left ventricular hypertrophy is unsatisfactory. In particular, none of the more recent and more sophisticated indexes is clearly superior to the Sokolow-Lyon index, which was developed in 1949 (Sokolow and Lyon, 1949) . Irrespective of the index used, the electrocardiogram is a poor screening tool to exclude left ventricular hypertrophy in hypertensive patients in primary and secondary care settings. It cannot be considered as a "SpPIn" (specific, positive, in) test for the diagnosis of left ventricular hypertrophy (Pewsner et al., 2004).

Bacharova commented the updating LVH recommendation published in 2009 as follow: "…the published ECG standards for LVH actually open more questions than provide recommendations (Ljuba, 2009)." AHA/ ACCF/HRS scientific statement has declared more than 30 criteria for left ventricular hypertrophy. The most commonly used diagnostic criteria for left ventricular hypertrophy (LVH) are based on measurements of QRS voltages. More recently, more complex criteria that are easily implemented with computerized recording and interpretation systems have been developed. The existence of many different criteria for diagnosing LVH makes clinical application more complex. The sensitivity of the various criteria is generally quite low (usually less than 50%), whereas, the specificity is quite high (often in the range of 85 to 90%). However, the sensitivity and specificity of each criterion is different. Thus, the diagnostic accuracy will depend on the specific criterion used. Because of these differences in sensitivity and specificity, patients who meet one set of criteria for LVH commonly do not meet other criteria. In a large group of patients with mild or moderate hypertension, only 11.2% of patients with LVH by either the Cornell voltage criterion or the Sokolow-Lyon criterion had LVH diagnosed by both criteria (Conway and Lip, 2001). In addition, the various criteria have different positive and negative predictive values in different patient population suggesting that the value of multiple criteria may be additive (Hancock et al., 2009).

We use the ECG data from HES, this epidemiological investigation for ophthalmological status. It is also an exploration for the relationship between eye diseases and cardiovascular conditions. Therefore, we have an opportunity for investigating the relationship between

Table 3. Evaluation of atherosclarotic factors with LVH indexes (N= 5209).

Factors	Cornell voltage-duration product			Sokolow-Lyon index		
	Positive (n= 607)	Negative (n= 4602)	P	Positive (n= 278)	Negative (n= 4931)	P
LVH index	2865.6±484.55	1422.0±472.32		39.52±1.82	23.52±0.82	
Age	52.93±12.41	52.02±12.19	0.22	52.47±12.27	52.01±12.20	0.39
Mean systolic BP	138.32±21.17	138.55±22.53	0.87	140.43±22.95	138.28±22.38	0.03*
Mean diastolic BP	76.51±11.26	77.52±12.29	0.18	77.88±12.31	77.41±12.24	0.38
Body mass index	24.21±3.02	24.50±3.72	0.22	24.45±3.27	24.49±3.74	0.83
Waist-hip-ratio	0.90±0.49	0.90±0.08	0.45	0.90±0.05	0.90±0.08	0.58
ABI-R	1.10±0.11	1.11±0.11	0.14	1.11±0.11	1.11±0.11	0.92
TBI-R	0.79±0.14	0.81±0.13	0.09	0.80±0.12	0.80±0.12	0.11
PWV-R	1559.75±358.84	1582.47±398.07	0.37	1391.11±16.12	1396.74±6.01	0.28
Glucose (mmol/l)	5.76±1.08	5.78±1.41	0.89	5.77±1.35	5.78±1.40	0.88
Urea nitrogen (mmol/l)	4.83±1.14	4.78±1.19	0.48	4.84±1.21	1.19±0.19	0.20
Creatine (mmol/l)	71.18±9.57	71.17±11.26	0.98	71.66±0.52	71.11±0.18	0.14
Total cholesterols (mmol/l)	4.58±0.95	4.60±0.96	0.85	4.68±1.02	4.58±0.95	0.04*
Total triglycerides (mmol/l)	1.50±0.98	1.52±1.05	0.74	1.51±0.05	1.52±1.02	0.42
High density lipoprotein (mmol/l)	1.29±0.28	1.27±0.28	0.37	1.29±0.13	1.28±0.05	0.16
Low density lipoprotein (mmol/l)	2.69±0.67	2.70±0.65	0.85	2.68±0.30	2.65±0.11	0.10
High sensitive C-reactive protein	2.32±5.06	2.15±4.87	0.64	2.75±0.27	2.75±0.08	0.62
Urea Uric acid	248.68±54.61	253.70±65.15	0.28	268.56±3.22	264.05±1.11	0.04*
Urea creatinine	89.43±63.46	86.23±118.66	0.68	86.47±2.50	82.17±1.98	0.56
Urea albumin	1.37±2.43	1.80±5.73	0.25	1.24±0.28	1.51±0.09	0.26
Urea uric acid	1374.9±705.81	1322.0±698.96	0.26	1689.93±30.52	1700.67±11.36	0.72

*****:P < 0.05.

ECG and many cardiovascular indexes and retinopathy without diabetes. The typical lesions of diabetic retinopathy (retinal microaneurysms, hemorrhages and cotton wool spots) are com-monly seen in persons without clinically diagnosed diabetes (Liang et al., 2008). According to our data, we find that those patients with retinopathy without diabetes have a high prevalence of ECG-LVH. LVH and retinopathy are considered as target organ damages, but we do not find regression relation between these situations. However, we really see the statistical difference both in Sokolow-Lyon index and Cornell product. Peng et al. (2010) reported that, the prevalence of retinopathy among participants without diabetes was 13.6% (95% confidence interval [CI], 12.6 to 14.6%). Independent risk factors associated with retinopathy were age (odds ratio, [OR], 1.02; 95% CI 1.01 to 1.03 per year increase), male gender (male vs. female, OR 1.27; 95% CI 1.08 to 1.49), higher FPG (OR 1.30; 95% CI 1.11 to 1.53 per mmol/l increase), higher systolic BP (OR 1.15; 95% CI 1.05 to 1.27 per 10 mmHg increase) and higher diastolic BP (OR 1.16; 95% CI 1.09 to 1.22 per 10 mmHg increase). So we think that, the differences might be based on the hypertension.

Life quality questionnaire includes the evaluation on mobility, self-care, daily activities, pain/ discomfort, the illness affecting oneself, relatives or someone needing you care. We find that in the ECG-LVH group, life quality scores have no statistical difference when Sokolow- Lyon index and Cornell product were used. But when we evaluated these branches separately, there was a strong relationship with the ECG-LVH indexes and the “pain/discomfort”, as well as with the “illness affecting the relatives”. While coming into the mental evaluation, Cornell product might be more suitable for screening ECG than Sokolow-Lyon index. However, this difference is not very obvious when the MMSE score is lower (MMSE< 15). It might because the senior group have more mental problems, as well as the cardiovascular changes.

Cornell voltage duration product gives us information beyond merely voltage changes. It also considers the conduction delay, which reflects the changes in electrical properties (Ljuba, 2009). With our study, when we consider the atherosclerotic factors, we find that the Cornell voltage duration product is difficult to find the differences between these risks in LVH and the ECG normal population. When we use another tool, Sokolow-Lyon index might be more useful in finding statistical differences in systolic blood pressure, total cholesterols and uric acid. This result reminds us of a word from the new statement 2009: “…none of the more recent and more sophisticated indexes is clearly superior to the Sokolow-Lyon index, which was developed in 1949” (Sokolow and Lyon, 1949).

This probably because this criterion is from the early epidemiological researches for cardiovascular diseases and prognostic evaluations. The multicentral, randomized, blinded and prospective trials should be designed for further information.

Conclusion

We should choose different criterion for different purposes. For atherosclerotic screening or epidemiological survey of cardiological diseases, the Sokolow-Lyon Index might be better. If we use the criterion for epidemiological ophthalmology such as our Handan eye study, both Sokolow-Lyon index and Cornell voltage duration product are usable. As for the evaluation of mental status and its relationship with the LVH risk factors, we might choose Cornell voltage duration product.

LIMITATION

Handan eye study is a well-designed epidemiological study for eye diseases and blindness. Its electro-cardiogram data gave us the opportunity for ECG-LVH evaluation in this cross-sectional study. However, it is not a prospective research for hypertension and other cardiovascular diseases and some important data, such as the intake of salt, are not available. Further prospective research in hypertension and cardiovascular diseases is necessary for achieving complete data. On the other hand, the population is only the rural areas in the northern China and the whole aspects of Chinese data need further research.

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