CLINICAL RESEARCH STUDY

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Limited Relationship of Voltage Criteria for Electrocardiogram Left Ventricular Hypertrophy to Cardiovascular Mortality

Le Dung Ha, MD,[a] Ayman Elbadawi, MD,[a] Victor F. Froelicher, MD[b]

[a]*Department of Internal Medicine, Rochester General Hospital, Rochester, NY;* [b]*The Division of Cardiovascular Medicine, Department of Medicine, Stanford School of Medicine, Stanford, Calif.*

ABSTRACT

BACKGROUND: Numerous methods have been proposed for diagnosing left ventricular hypertrophy using the electrocardiogram. They have limited sensitivity for recognizing pathological hypertrophy, at least in part due to their inability to distinguish pathological from physiological hypertrophy. Our objective is to compare the major electrocardiogram–left ventricular hypertrophy criteria using cardiovascular mortality as a surrogate for pathological hypertrophy.

METHODS: This study was a retrospective analysis of 16,253 veterans < 56 years of age seen at a large Veterans Affairs Medical Center from 1987 to 1999 and followed a median of 17.8 years for cardiovascular mortality. Receiver operating characteristics and Cox hazard survival techniques were applied.

RESULTS: Of the 16,253 veterans included in our target population, the mean age was 43 years, 8.6% were female, 33.5% met criteria for electrocardiogram–left ventricular hypertrophy, and there were 744 cardiovascular deaths (annual cardiovascular mortality 0.25%). Receiver operating characteristic analysis demonstrated that the greatest area under the curve (AUC) for classification of cardiovascular death was obtained using the Romhilt-Estes score (0.63; 95% confidence interval, 0.61-0.65). Most of the voltage-only criteria had nondiagnostic area under the curves, with the Cornell being the best at 0.59 (95% confidence interval, 0.57-0.62). When the components of the Romhilt-Estes score were examined using step-wise Wald analysis, the voltage criteria dropped from the model. The Romhilt-Estes score ≥ 4, the Cornell, and the Peguero had the highest association with cardiovascular mortality (adjusted hazard ratios 2.2, 2.0, and 2.1, consecutively).

CONCLUSION: None of the electrocardiogram leads with voltage criteria exhibited sufficient classification power for clinical use.

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KEYWORDS: Cardiovascular mortality; Electrocardiogram; Left ventricular hypertrophy; Voltage criteria

INTRODUCTION

For decades, medical students and physicians have had to memorize voltage criteria for diagnosing left ventricular hypertrophy (**Table 1**). Furthermore, automated electrocardiogram programs generate the statement "left ventricular hypertrophy" based on these criteria. This is the state of practice despite their low sensitivity for morphological left ventricular hypertrophy and their failure to distinguish pathological from physiological left ventricular hypertrophy. Recently, Peguero et al presented a new electrocardiogram voltage schema that exhibited twice the sensitivity for echocardiographic left ventricular hypertrophy as the Sokolow-Lyons or Cornell voltage scores.[1]

While electrocardiogram–left ventricular hypertrophy and anatomic left ventricular hypertrophy may be separate entities,[2] cardiovascular deaths remain an appropriate marker of pathological left ventricular hypertrophy. In a prior evaluation of the prognostic value of the major electrocardiogram criteria for left ventricular hypertrophy, we found that the voltage-only scores performed poorly compared with the scores

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Requests for reprints should be addressed to Le Dung Ha, MD, Rochester General Hospital, 1425 Portland Avenue, Rochester, NY 14621.

E-mail address: ledung.ha@rochesterregional.org

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that included other electrocardiogram features or demographics.[3] Given the availability of a new score with possible increased sensitivity, we conducted this study in a younger population with a longer follow-up than the previous study to revisit this issue.

METHODS

Population

This was a retrospective study including all patients younger than 56 years who had a resting electrocardiogram performed at Palo Alto Veterans Administration Health Care System from March 1987 to December 1999. If a patient had more than one electrocardiogram in the database, we considered only the initial study. All the electrocardiograms were recorded and stored in a centralized computerized electrocardiography MUSE system and 12SL automated analysis program (GE Healthcare, Wauwatosa, Wis). Electrocardiograms were most often obtained as part of a screening of patients initiating care. Additional clinical data about symptomatology, comorbidities, and diagnosis were not available. All computerized interpretations were over-read by an experienced cardiologist prior to being recorded into the database.

Of these 21,169 electrocardiograms available, those from patients with atrial fibrillation (n = 120, 0.5%), pacemakers (n = 21, 0.1%), Wolff-Parkinson-White pattern (n = 32, 0.1%), and acute myocardial infarction (n = 10, 0.05%) were excluded. To avoid the probability of confounding by catabolic complicating illness, we excluded electrocardiograms from patients with body mass index ≤ 20 (n = 4733, 22.3%). The target population included 14,845 males and 1408 females between 20 and 55 years of age.

CLINICAL SIGNIFICANCE

- Most of the electrocardiogram voltage-only left ventricular hypertrophy criteria had non-diagnostic Area Under the Curve.
- The clinical use of these voltage-only left ventricular hypertrophy criteria must be reconsidered and these criteria should not be in the statement libraries of automated electrocardiogram machines.
- The electrocardiogram leads with voltage criteria with the greatest association with cardiovascular mortality were aVL (R wave) and V3 (S wave).

Electrocardiogram Criteria

Analysis included 17 different criteria to identify electrocardiogram–left ventricular hypertrophy in our study cohort. There were 14 voltage-only criteria and 3 composite criteria (2 point-score systems and 1 regression equation criteria) (**Table 1**). These included Minnesota code 3.1,[4] Sokolow-Lyon,[5] unadjusted Cornell voltages,[6] Framingham-adjusted Cornell voltages,[7] Lewis index,[8] Gubner-Ungerleider,[9] sum of 12 leads,[10] Peguero,[1] Cornell products,[11] 12-lead products,[10] Perugia score,[12] Romhilt-Estes score,[13] and the Rautaharju left ventricular mass index equation.[14]

Outcomes

The California Department of Health Care Services and Social Security Death Index were used to ascertain the vital status of each patient as of April 2013. Cardiovascular causes of death were defined according to the International Classification of Diseases, Ninth Revision (ICD-9) code numbers 390-459. Accuracy of all causes of death was confirmed using the Veterans Affairs computerized patient record system by 2 physicians blinded to the electrocardiogram results. Causes of deaths were identified through review of the death indices and charts from the electronic medical record system. Clinical visits and testing, problem lists, autopsies, and discharge or death summaries were used to specify cases of cardiovascular mortality.

Statistical Analysis

Baseline Characteristics. Baseline characteristics were compared between patients with and without cardiovascular mortality during the study period using univariate Cox regression analysis. Continuous variables were expressed as mean (M) and standard deviation (SD). Dichotomous variables were expressed as number (n) and percentage (%). The effect size of the differences was summarized using unadjusted hazard ratio (HR) and 95% confidence intervals (CI). Annual mortality rate was calculated using the life table in SPSS (IBM, Armonk, NY).

ROC-AUC. To evaluate the discriminatory performance of the electrocardiogram–left ventricular hypertrophy criteria in predicting cardiovascular mortality, area under the curve ([AUC] with 95% CI) of receiver operating characteristic (ROC) for time-based data was used use in cases of quantitative variables.[15] This could be used to determine optimal cut points for continuous variables, while the new Peguero criteria[1] required using the Olshen survival tree, which is a specialized variant of the classification and regression trees ("rpart" package in R).

Survival Analysis. Cox regression analysis was performed using HR and 95% CI, with cardiovascular death as the outcome. Unadjusted and adjusted HRs were calculated from Cox regression to quantify the risk of cardiovascular mortality associated with different electrocardiogram–left ventricular hypertrophy criteria.

To compare the hazard ratios of different criteria, they were entered in a model, and Wald test was implemented to compare the betas. The proportional hazards assumption in the Cox model was assessed using log-log plot of survival and Schoenfeld residual test. All proportional hazards assumptions were appropriate. Statistical analyses were performed using SPSS. *P*-values < .05 were considered statistically significant. Cox proportional hazards regression analysis was used