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Seamens' Sign: A Novel Electrocardiogram Prediction Tool for Left Ventricular Hypertrophy

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Abstract

Study Objective:

We developed a novel, quick, easy to use electrocardiogram (ECG) screening criterion (Seamens' Sign) for left ventricular hypertrophy (LVH). This new criterion was defined as the presence of QRS complexes touching or overlapping in two contiguous precordial leads.

Methods:

This study was a retrospective chart review of 2184 patient records. The primary outcome was whether Seamens' Sign was noninferior in confirming LVH compared to other common criteria. Test characteristics were calculated for each of the LVH criteria. Inter-rater agreement was assessed on a random sample using Cohen's Kappa.

Results:

Median age was 63, 52% of patients were male and there was a 35% prevalence of LVH by transthoracic echocardiogram (TTE). Nine percent were positive for LVH on ECG based on Seamens' Sign. Seamens' Sign had a specificity of 0.92. Tests assessing noninferiority indicated Seamens' Sign was non-inferior to all criteria ($p < 0.001$) except for Cornell criterion for women ($p = 0.98$). Seamens' Sign had 90% (0.81-1.00) inter-rater agreement, the highest of all criteria in this study.

Conclusion:

When compared to both the Sokolow-Lyon criteria and the Cornell criterion for men, Seamens' Sign is noninferior in ruling in LVH on ECG. Additionally, Seamens' Sign has higher inter-rater agreement compared to both Sokolow-Lyon criteria as well as the Cornell criteria for men and women, perhaps related to its ease of use.

1.0 Background

Patients with left ventricular hypertrophy (LVH) diagnosed by electrocardiogram (ECG) have increased mortality and a higher risk for life-threatening cardiovascular disease, most commonly coronary artery disease in men and heart failure in women., LVH is commonly diagnosed via ECG in the emergency department (ED), often in cardiac workup or incidentally. These LVH diagnoses provide evidence of patients' overall cardiovascular health and inform cardiac risk management and stratification.

The process of diagnosing LVH is multi-faceted. Cardiac echocardiography or left ventricular mass measurements via cardiac magnetic resonance imaging (MRI) are the gold standards,. However, widespread LVH screening via these methods is neither feasible nor cost effective. ECGs performed in the ED setting offer an opportunity to identify patients with increased risk for cardiac mortality and who are candidates for potential risk-modifying therapy. Despite the importance of efficient, accurate LVH prediction based on ECGs, commonly used methods have known diagnostic test inaccuracies and are challenging to use.

Most current criteria require measuring or adding varying lead voltages, and may be complicated by risk of calculation errors. There are numerous ECG criteria for identifying LVH, with varying tests characteristics influenced by underlying cardiac conduction defects, gender, race, and body habitus.”

Ultimately, ECG diagnostic criteria for LVH are clinically lacking. Though many attempts at defining more sensitive and specific ECG criteria for LVH have been proposed, none approach the accuracy of gold-standard imaging modalities. These proposed criteria generally increase complexity to marginally improve sensitivity and/or specificity, creating a barrier to quick application in the ED setting.

Instead of more complex ECG criteria, we propose a novel, quick, and easily recognizable screening criterion for LVH can be learned with little memorization and applied in a fast-paced setting. The proposed criterion— “Seamens’ Sign”—involves one question: do any of the QRS complexes in the precordial leads of a standard 12-lead ECG touch or cross another QRS complex (e.g., V1 QRS complex touching/crossing V2 QRS complex) (Fig. 1)?

From an electrophysiologic standpoint, many reasons explain why precordial lead QRS complex touching/overlap works for LVH detection. Typical, non-pathologic R wave progression in the precordial leads shows that as the electrical signal passes from the sinoatrial node towards the apex of the left ventricle, prominent S waves (overall negative deflection) in V1 and V2 transition to predominant R waves (overall positive deflection) in V5 and V6. As the left ventricle hypertrophies, changes occur leading to an electrical vector of greater magnitude, translating to increased amplitude of the S and R waves in the precordial leads, often leading to the precordial QRS complexes touching or overlapping.’

In this study, we evaluated the test characteristics of the proposed Seamens’ Sign and compared its ability to confirm an LVH diagnosis against three of the most used voltage criteria today (two Sokolow-Lyon criteria and the Cornell Criteria).

2.0 Methods

2.1 Study Design

This study was an electronic health record (EHR) retrospective chart review at a quaternary care academic medical center. The data collection period included clinical tests performed 5 July 2019 through 14 January 2020 as part of routine ED care.

2.2 Eligibility

A query of the EHR was performed, identifying patients with both an ECG and a transthoracic echocardiogram (TTE) performed within 90 days of each other. No patients were excluded prior to data analysis on the basis of age, ethnicity, comorbidities, co-existing cardiac diagnoses evident on ECG or TTE, or other clinical factors.

2.3 Data Collection & ECG Coding

Total sample size for chart review was determined based on the number of subjects needed to estimate the sensitivity of Seamens' Sign to a pre-specified margin of error. A total of 2184 patient records were reviewed based on estimating a hypothesized sensitivity of 65% to a 2% margin of error. Data gathered during the initial EHR query included age, sex, ECG time/date, and TTE time/date. Each patient chart was assembled by an initial set of reviewers (primarily third year medical students), and assigned a random study number. They downloaded a copy of the ECG labeled with the study number and with all patient identifiers removed. They reviewed the TTE report and recorded whether or not LVH was identified. LVH was defined as any mention of the patient having concentric LVH in the TTE report. Septal or other focal hypertrophy was not considered LVH.

A second, independent set of blinded reviewers (Emergency Medicine residents) reviewed each ECG for signs of LVH based on two Sokolow-Lyon criteria, the Cornell criteria, and the study criterion, Seamens' Sign. The first criterion, noted as the Sokolow-Lyon 1 criterion (SL-1) was defined as the S wave in lead V1 plus the R wave in lead V5 or V6 (using larger R wave in V5 or V6) being greater than or equal to 35mm. The second Sokolow-Lyon criterion, noted as Sokolow-Lyon 2 criterion (SL-2), was defined as the R wave in lead aVL being greater than or equal to 11mm. The Cornell criteria were defined as the S wave in lead V3 plus the R wave in lead aVL being greater than 28mm in males or greater than 20mm in females. These criteria's test characteristics were compared against the test characteristics for the proposed new criterion, Seamens' Sign. This new criterion was defined as the presence of QRS complexes touching or overlapping in two contiguous precordial leads (lead V1 QRS complex touching/crossing lead V2 QRS complex, or lead V2 QRS complex touching/crossing lead V3 QRS complex, or lead V4 QRS complex touching/crossing lead V5 QRS complex, or lead V5 QRS complex touching/crossing lead V6 QRS complex).

2.4 Outcome Measures

The primary outcome was determining whether Seamens' Sign was noninferior in confirming LVH compared to the other criteria.

2.5 Analysis

Diagnosis of concentric LVH by TTE was considered the gold standard against which the various ECG criteria for LVH were compared to determine sensitivity and specificity.

Descriptive statistics of demographic and clinical characteristics were computed for the study population. Test characteristics, including sensitivity, specificity, and positive and negative predictive values, along with their 95% confidence intervals, were calculated for each of the LVH criteria. Non-inferiority of Seamens' Sign criterion compared to the Cornell and Sokolow-Lyon criteria was evaluated using a method designed for paired binary data. The margin of non-inferiority was pre-specified at 5% (p = 0.05). To compare Cornell criteria for men and women to those with Seamens' Sign, only men with Seamens' Sign were compared to other men meeting Cornell criteria, and the same method was used for women. To ensure validity of reviewer ECG coding and assess ease of interpretation, inter-rater agreement was assessed on a random sample using Cohen's Kappa with the 95% confidence intervals. All statistical analyses were performed using R statistical programming language, Version 3.5.2.

3.0 Results

3.1 Patient Characteristics

Patient characteristics are listed in Table 1. Median age was 63, 52% of patients were male and there was a 35% prevalence of LVH by TTE. The vast majority of TTEs were performed within 1 day of ECGs, with the median of 1 day, and the interquartile range of 0 to 21 days. Nine percent were positive for LVH on ECG based on Seamens' Sign, and 3% and 7% were positive for LVH on ECG based on Sokolow-Lyon 1 and Sokolow-Lyon 2 criteria, respectively. There were 7% of men and 13% of women positive for LVH on ECG based on Cornell criteria.

Table 1

Descriptive statistics on demographic and clinical characteristics of the cohort. N is the number of non-missing values. Numbers after proportions are frequencies, with the exception of age and ECG to TTE. Age and ECG to TTE are reported as the median, with following numbers the lower and upper interquartile for these continuous variables.

	N	N = 2184
Age	2184	63 (51, 73)
Sex	2184	
Male		52% (1135)
Female		48% (1049)
TTE for LVH (gold standard)	2184	
No		65% (1428)
Yes		35% (756)
ECG to TTE (days)	2184	1 (0, 21)
Seamens' Sign positive for LVH	2184	
No		91% (1994)
Yes		9% (190)
Sokolow-Lyon 1 positive for LVH	2184	
No		97% (2113)
Yes		3% (71)
Sokolow-Lyon 2 positive for LVH	2184	
No		93% (2037)
Yes		7% (147)
Cornell (overall) positive for LVH	2184	
No		90% (1971)
Yes		10% (213)
Cornell (men) positive for LVH	1135	
No		93% (1056)
Yes		7% (79)

	N
Cornell (women) positive for LVH	1049
No	87% (914)
Yes	13% (135)

3.2 Sensitivity and Specificity

Test characteristics are presented in Table 2. Specificities ranged from 0.89 for the Cornell criterion for women to 0.98 for the Sokolow-Lyon 1 criterion, with Seamens' Sign having a specificity of 0.92.

Table 2
Test characteristics for Seamens' Sign criterion, Sokolow-Lyon 1 (SL-1) and 2 (SL-2) criteria, and Cornell criteria for diagnosing left ventricular hypertrophy from electrocardiograms.

	Sensitivity		**Specificity**		**PPV**		**NPV**	
Test	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Seamens' Sign	0.11	(0.09, 0.13)	0.92	(0.91, 0.94)	0.43	(0.36, 0.51)	0.66	(0.64, 0.68)
SL-1	0.05	(0.03, 0.07)	0.98	(0.97, 0.98)	0.51	(0.39, 0.63)	0.66	(0.64, 0.68)
SL-2	0.08	(0.06, 0.10)	0.94	(0.93, 0.95)	0.41	(0.33, 0.50)	0.66	(0.64, 0.68)
Cornell Overall	0.13	(0.11, 0.15)	0.92	(0.90, 0.93)	0.46	(0.39, 0.52)	0.67	(0.64, 0.69)
Cornell Men	0.09	(0.07, 0.12)	0.94	(0.92, 0.96)	0.51	(0.39, 0.62)	0.62	(0.59, 0.65)
Cornell Women	0.18	(0.14, 0.23)	0.89	(0.87, 0.91)	0.42	(0.34, 0.51)	0.71	(0.68, 0.74)

3.4 Non-Inferiority

Tests assessing noninferiority indicated Seamens' Sign was non-inferior to all criteria ($p < 0.001$) except for Cornell criterion for women ($p = 0.98$) (Table 3).

Table 3
p-values for tests assessing non-inferiority of Seamens' Sign when compared to other commonly used tests.

Comparison	P
Sokolow-Lyon 1	< 0.001
Sokolow-Lyon 2	< 0.001
Cornell Overall	< 0.001
Cornell Men	< 0.001
Cornell Women	0.98

3.3 Inter-Rater Agreement

Inter-rater agreement was assessed on 250 subjects using Cohen's Kappa statistic and a 95% confidence interval (Table 4). Seamens' Sign had 90% (0.81-1.00) agreement, the highest of all criteria, attributed to its quick application and ease of use. Sokolow-Lyon 1 and Sokolow-Lyon 2 had inter-rater agreement of 65% (0.40–0.91) and 87% (0.75-1.00) respectively. Sokolow-Lyon 1 likely has lower inter-rater agreement secondary to multiple leads used and subjectivity in selecting the R wave in lead V5 or V6. Cornell criteria for men and women had inter-rater agreements of 76% (0.56–0.96) and 79% (0.62–0.97), respectively.

Table 4
Inter-rater agreement using Cohen's Kappa with 95% confidence interval.

Test	Kappa	95% CI
Seamens' Sign	0.9	(0.81, 1.00)
Sokolow-Lyon 1	0.65	(0.40, 0.91)
Sokolow-Lyon 2	0.87	(0.75, 1.00)
Cornell Overall	0.82	(0.69, 0.94)
Cornell (Men)	0.76	(0.56, 0.96)
Cornell (Women)	0.79	(0.62, 0.97)

4.0 Discussion

While modalities other than ECG are the gold-standard for diagnosing LVH, it is important to account for their difficulty and cost compared to the quick, easy to obtain, and inexpensive ECG, particularly in emergency care settings. Furthermore, there are data suggesting LVH diagnosed by ECG criteria represents a clinically distinct entity, and has been associated with increased mortality and other pathologic conditions. This furthers the argument of the importance of fast, reliable methods of diagnosing LVH by ECG.

This analysis suggests Seamens’ Sign is non-inferior to other methods of evaluating LVH on ECG, and has high inter-rater agreement. It is easy to perform quickly without a measurement device or need for any calculations at all. Given these findings, we believe that Seamens’ Sign is easily applicable in emergency care settings and can facilitate the diagnosis of LVH, potentially leading to decreased cardiac morbidity and mortality.

4.1 Strengths

This is a large study comparing test characteristics of multiple criteria to Seamens' Sign.

Three of the most widely used criteria were chosen to model real-world application. Compared to most prior studies, the number of subjects analyzed was larger. Of the prior 14 studies analyzing ECG diagnosis of LVH, enrollment ranged from 94 to 5608 patients; this study is the third largest. Those interpreting ECGs were blinded from the TTE results to remove any bias. The proliferative phase of cardiac remodeling takes place within the first 2–7 days after a myocardial infarction, transitioning to the maturing phase around day 7. Based on these findings, a 90-day limit on the time difference between the TTE and ECG dates was placed to reduce the likelihood of cardiac remodeling affecting results. The majority of the ECGs and TTEs were performed within 1 day of each other, limiting the chances of cardiac remodeling affecting the ECG or TTE.

4.2 Limitations

While Seamens’ Sign is a quick, effective, reliable alternative to other criteria for diagnosing LVH on ECG, there are study limitations. All ECGs were included, without removal of bundle branch blocks or other abnormal findings that could alter the results. However, this limitation was applied across all criteria in the study, helping to eliminate any differences in their application. Also, with the exception of the Cornell criteria which differentiates between sexes, we did not differentiate the application of the other criteria based on sex. This could hide differences in application of the criteria between sexes, but stays true to original application of these criteria. There were no changes in application of criteria based on age. There are known differences in ECG appearance based on age, including potential QRS amplitude changes. Finally, since this was a retrospective study, there were multiple providers obtaining ECGs, multiple echocardiographers performing the TTEs, and multiple cardiologists reading the TTEs, which could lead to variability in ECG and TTE acquisition, interpretation, and reporting of LVH.

5.0 Conclusion

When compared to both the Sokolow-Lyon criteria and the Cornell criterion for men, Seamens’ Sign is noninferior in confirming LVH on ECG. Additionally, Seamens’ Sign has higher inter-rater agreement compared to both Sokolow-Lyon criteria as well as the Cornell criteria for men and women, possibly related to its ease of use.

6.0 Declarations

6.1 Ethics approval and consent to participate

This study (IRB#200150) was approved by the Vanderbilt Institutional Review Board and Human Research Protections Program as an exempt study that poses minimal risk to participants given it only involved retrospective chart review. The informed consent for this study is waived by the Vanderbilt Institutional Review Board due to retrospective nature. All methods were performed in accordance with the relevant guidelines and regulations.

6.2 Consent for publication

The informed consent for this study is waived by the Vanderbilt Institutional Review Board due to retrospective nature.

6.3 Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due being secured in a private, password protected, Vanderbilt University Medical Center (VUMC) repository only available to VUMC employees, but are available from the corresponding author on reasonable request.

6.4 Competing interests

The authors declare that they have no competing interests.

6.5 Funding

There was no internal or external funding for this research study.

6.6 Authors' contributions

PWW, NM, ABS, CAJ, and CS conceived and designed the study. PWW, NM, and ABS were responsible for drafting and obtaining IRB approval. PWW and NM supervised data collection and conduction of the study. CAJ provided statistical advice on study design and analyzed the data. JBS, EH, CM, TR, LCW, TP, RP, AA, OH, JO, and AK were the primary initial chart reviewers. CLF, NS, and BR were the second set of blinded reviewers. PWW drafted the manuscript, and all authors contributed substantially to its revision. PWW takes responsibility for the paper as a whole.

6.7 Acknowledgements

Not applicable

7.0 List Of Abbreviations

ECG—Electrocardiogram

ED—Emergency department

EHR—Electronic health record

LVH—Left ventricular hypertrophy

MRI—Magnetic resonance imaging

NPV—Negative predictive value

PPV—Positive predictive value

SL-1—Sokolow-Lyon 1 criterion

SL-2—Sokolow-Lyon 2 criterion

TTE—Transthoracic echocardiogram

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Figures

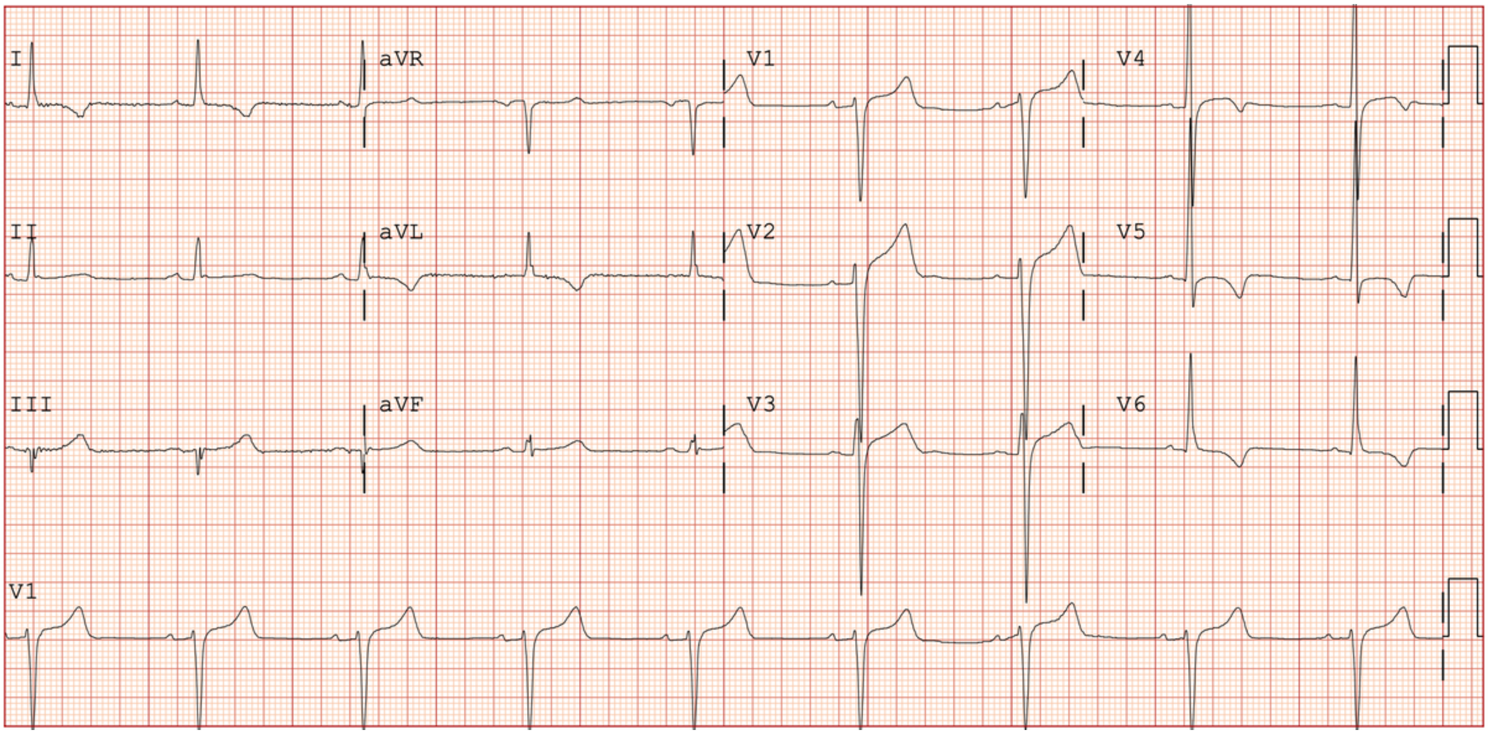

Figure 1

Standard 12-lead electrocardiogram demonstrating Seamens' Sign with precordial QRS complexes overlapping and/or touching. This is best seen with V2 touching/overlapping V3, as well as V4 touching/overlapping V5.