

Accuracy of Electrocardiographic Criteria in the Diagnosis of Left Ventricular Hypertrophy in Complete Left Bundle Branch Block: A Systematic Review with Meta-analysis

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ABSTRACT

Introduction: Left Ventricular Hypertrophy (LVH) is commonly present in patients with complete Left Bundle Branch Block (LBBB) and has significant prognostic implications. The LBBB fundamentally alters ventricular depolarisation and repolarisation patterns, complicating the Electrocardiography (ECG) diagnosis of LVH. Despite decades of research, accurate diagnostic criteria remain unclear.

Aim: A systematic review and meta-analysis was conducted to evaluate the accuracy and clinical utility of various electrocardiographic criteria in diagnosing LVH in patients with complete LBBB.

Materials and Methods: A search was performed using PubMed and institutional databases from 1969 to August 2024 for studies evaluating ECG criteria for LVH diagnosis in LBBB patients, using echocardiography, Cardiac Magnetic Resonance Imaging (CMRI), or autopsy as reference standards. Sixty-four ECG criteria were analysed across 15 studies comprising 1,595 patients. Two reviewers independently

selected studies, extracted data, and assessed methodological quality using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. A random-effects meta-analysis was conducted to calculate pooled sensitivity, specificity, likelihood ratios, and Diagnostic Odds Ratios (DOR). Studies were stratified by cumulative sample size, and heterogeneity was assessed using the I^2 statistic.

Results: Among the parameters evaluated in studies with sample sizes exceeding 400 patients, Left Atrial Enlargement (LAE) criteria demonstrated the highest DOR and predictive accuracy. However, decision-curve analysis could not demonstrate the clinical utility of any ECG criteria for adequately diagnosing LVH in the study population.

Conclusion: No ECG criteria demonstrated significant diagnostic accuracy for LVH in patients with LBBB. Therefore, multimodal diagnostic approaches incorporating clinical assessment, risk stratification, and confirmatory imaging are essential for accurate LVH diagnosis in patients with complete LBBB in clinical practice, in addition to ECG.

Keywords: Cardiac conduction defects, Cardiac hypertrophy, Diagnostic validity, Left atrial enlargement, Left ventricular enlargement

INTRODUCTION

The diagnosis of LVH in patients with complete LBBB poses a significant clinical challenge and has important implications [1-4]. Multiple studies [1-6] have shown that anatomic LVH is common in patients with LBBB, with its prevalence increasing alongside advancing age and cardiovascular co-morbidities. In LBBB, abnormal intraventricular conduction fundamentally alters cardiac electrical patterns. QRS duration exceeds 120 ms, ventricular activation sequences are delayed, and ST segments and T waves undergo secondary changes [1]. These conduction abnormalities produce characteristic voltage redistributions, including increased QRS amplitude in leads V1-V2 and decreased amplitude in V5-V6 [1], thereby compromising the reliability of conventional voltage-based LVH criteria. LVH frequently coexists with LBBB and represents an independent predictor of cardiovascular morbidity and mortality [1], making accurate diagnosis essential [4].

Electrocardiography is the most widely available non-invasive diagnostic tool for LVH [4]. However, its utility in detecting LVH in patients with LBBB remains questionable. Expert opinions differ regarding the use of ECG to diagnose LVH in the presence of LBBB. Some authors suggest that ECG criteria can be applied to a certain extent when LBBB is present [2], while others claim that ECG criteria are as reliable as in normal conduction, even in the presence of LBBB [3-5]. Conversely, several authors believe that ECG is not an ideal diagnostic tool [6], as it poorly identifies

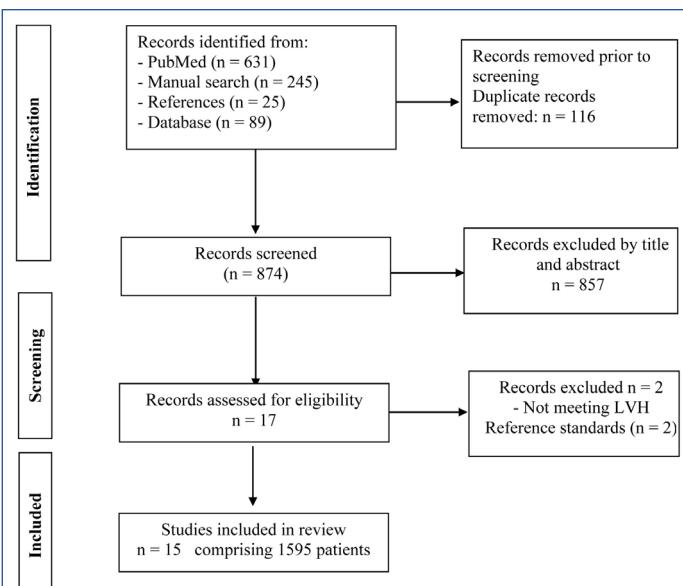
increased Left Ventricular (LV) mass [7] and shows weak correlation between anatomical LVH and ECG-based LVH criteria [8]. Some researchers argue that attempting to diagnose LVH using ECG in LBBB is futile [7]. Numerous novel criteria have been proposed to improve the diagnostic accuracy of ECG for LVH in LBBB patients [9-13]. Hence, the present study aims to analyse selected available studies to assess the accuracy of individual ECG parameters and their clinical utility for diagnosing LVH in patients with LBBB.

MATERIALS AND METHODS

The present systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The PRISMA flow diagram is depicted in [Table/Fig-1].

Data Sources and Search Strategy

Relevant published articles were searched in PubMed and through free-text searches. The keywords used were: LVH, complete LBBB, electrocardiographic parameters, and ECG. No filters were applied. Additional sources included manual searching of references, textbooks, institutional databases, and medical university repositories from 1969 to 2024. Only studies published in English, including both prospective and retrospective designs, were considered. The reference lists of included articles and related reviews were also screened for additional studies. All searches were re-run before the final analysis.



[Table/Fig-1]: PRISMA flow diagram showing systematic review study selection, screening phases, exclusion criteria application, and final study inclusion from 1969-2024 literature search across multiple databases.

PICOS Framework

- Population:** Adult patients with a confirmed diagnosis of complete LBBB
- Intervention/Index Test:** ECG voltage criteria used for diagnosing LVH in complete LBBB
- Comparison/Reference Standard:** Echocardiography, cardiac MRI, or autopsy as the gold standard to diagnose LVH
- Outcomes:** Sensitivity, specificity, positive and negative likelihood ratios, DOR, positive and negative predictive values, predictive accuracy, Area Under the receiver-operating characteristic Curve (AUC), and decision curve analysis
- Study Design:** Prospective and retrospective studies published in English from 1969 to 2024

Study Selection and Eligibility Criteria

Inclusion criteria: Prospective and retrospective studies in English, published between 1969 and 2024, reporting the sensitivity and specificity of electrocardiographic criteria for diagnosing LVH in patients with complete LBBB using echocardiography, CMRI, or autopsy as the reference gold standard.

Exclusion criteria: Isolated case reports, case series, manuscripts containing only abstracts, and animal studies were excluded.

Quality assessment: Two reviewers independently screened records and extracted data using a standardised form. The methodological quality and risk of bias of the 15 included studies were assessed using the QUADAS-2 tool [14] (Whiting PF et al., 2011). Four domains were evaluated-patient selection, index test, reference standard, and flow and timing-and were risk-stratified as low, moderate, or high risk.

STATISTICAL ANALYSIS

The relevant data for this study were collected and organised into a master chart using Microsoft Excel. For each ECG criterion, sensitivity and specificity were calculated to assess diagnostic accuracy. Ninety-five percent confidence intervals were estimated using the Wilson score method to account for uncertainty around these measures. A Summary Receiver Operating Characteristic curve (SROC) curve was plotted, and the Area Under the Curve (AUC) was calculated to determine overall test performance. DCA was performed for threshold probabilities between 0 and 0.5 to evaluate the potential clinical usefulness of each criterion. Forest plots of sensitivity and specificity with 95% confidence intervals were constructed. Potential small-study effects and publication bias were assessed using Deeks' funnel plot asymmetry test, with a p-value<0.10 interpreted as evidence of potential publication bias. All analyses and figures were generated using Python software (version 3.11) with the following packages: pandas, numpy, matplotlib, scikit-learn, and statsmodels. Microsoft Excel 11.0 was used for tables and supplementary calculations.

RESULTS

A total of 990 manuscripts were initially retrieved. After removing duplicate records and excluding studies based on title and abstract screening, 17 studies remained and were assessed for eligibility. Of these, two studies were excluded because they did not use any of the specified reference standards for LVH diagnosis. Finally, 15 studies [1,3-13,15-17] were included in the meta-analysis, comprising a total of 1,595 patients, as shown in [Table/Fig-1].

A total of 64 ECG criteria were analysed for their sensitivity and specificity, and average values of sensitivity and specificity were calculated for each parameter. The sample size represented by each ECG criterion was also calculated. Of the 64 ECG criteria, the distribution was as follows: 19 criteria had a cumulative sample size of 400 patients or more, 2 criteria had a sample size between 300 and 400 patients, and 10 criteria had a sample size between 200 and 300 patients. The remaining 33 criteria had sample sizes fewer than 200 patients and were therefore not tabulated due to their smaller sample size. These samples were analysed separately with respect to their average sensitivity, specificity, Positive Likelihood Ratio (LR+), Negative Likelihood Ratio (LR-), DOR, Positive Predictive Value (PPV), Negative Predictive Value (NPV), predictive accuracy, SROC analysis, and decision curve analysis to assess their utility for the diagnosis of LVH in patients with LBBB. Selected diagnostic ECG criteria and their thresholds are presented in [Table/Fig-2].

The characteristics of the included studies are summarised in [Table/Fig-3] [1,3-13,15-17]. [Table/Fig-4-9] depict the number of patients represented by individual criteria from all studies pooled in the meta-analysis. The results are tabulated in [Table/Fig-4-9]. Three studies [1,5,8] reported autopsy findings, one study [6] provided CMRI data, and the remaining studies [3-4,7,9-13,15-17] used echocardiography for LVH assessment. The prevalence of LVH ranged from 37% to 95.3% (average 63.6%). The mean age of study participants ranged from 39±14 to 78.4 years, with

Criteria	Formula	LVH definition
Sokolow-LYON	SV1+R (V5 or V6)	>35 mm
Lewis Index	(RI+SI)-(RIII+SI)	≥17 mm
Klien	SV2+RV6	>45 mm
Kafka	RAVL >11 mm, QRS axis ≤40 degrees, SV1+RV5 or RV6 >40 mm, SV2 ≥30 mm and SV3≥25 mm	Any of the 4 parameters in a cumulative fashion
Romhilt Estes	Points	≥5 points
Gubnierz-Ungerleider	RI+SI	>25 mm
Cornell Voltage	RAVL+SV3	≥28 mm (Male), ≥20 mm (female)
Dalfo	RAVL+SV3	≥16 mm (Male) ≥14 mm (Female)
Sokolow-Lyon VDP	SV1+max (RV5orV6) × QRS Duration	>367.4 mV ms (men), 322.4 mV ms (women)

Cornell's VDP	Men: RaVL+SV3 × QRS Duration Women: (RaVL+SV3+.6 mV) × QRS Duration	>244 mV ms
Gubnier-Ungerleider VDP	Gubnier × QRS Duration	>207 mV ms
12-Lead QRS VDP	12 lead QRS area	>2348.8 mV ms (men), >322.4 mV ms (women)
RaVL VDP	RaVL × QRS Duration	>103 mV ms
Total 12 Lead ECG QRS amplitude	R+S (or Q, whichever is higher in all the Leads)	>19 530 mV (men),>18499 mV (women)
Perugia	SV3+RaVL>24 mm (men) or >20 mm (women), or LV pressure overload pattern, or Romhilt Estes ≥5 points	Any of the three variables.
Peguero-lo presti	Max S+SV4	≥ 23 mm (women), 28 mm (Men)

[Table/Fig-2]: Definitions of electrocardiographic criteria and diagnostic thresholds for LVH detection. Standard and novel ECG parameters with their mathematical formulas and cut-off values for LVH diagnosis, including voltage-based criteria, duration-based criteria, and composite scoring systems.

LVH: Left ventricular hypertrophy; VDP: Voltage-duration product; QRS: Electrocardiographic complex representing ventricular depolarisation; RaVL: R-wave amplitude in lead aVL (augmented vector left); SV1, SV2, SV3: S-wave amplitude in leads V1, V2, V3 respectively; RV5, RV6: R-wave amplitude in leads V5, V6 respectively

S No	Authors name	Study design	Sample size (n)	Year of publishing	Place of Study	Reference/Gold Standard	LVH Criteria	Men	Women	Mean Age (Years)	LVH (%)
1	Peterson GV et al., [8]	R	50	1971	USA	Autopsy	LV thickness>13 mm (LVH)	27	23	75.7	80%
2	Zmyslinski RW et al., [5]	R	43	1980	USA	Autopsy	Heart weight 2SD above the normal mean	32	11	64.95	95.30%
3	Havelda CJ et al., [1]	R	70	1982	USA	Autopsy	>180 gm	0	0	67.1±7.8 LBBB LAXD 64.6±11.6 LBBB Normal axis	70%
4	Noble LM et al., [15]	R	30	1984	USA	ECHO	LV mass >215 gm	All males	0	68	89.30%
5	Haskell RJ et al., [16]	P	37	1987	USA	ECHO	>281 gm LVH	14	23	60.7±12%	54%
6	Kafka H et al., [3]	P	125	1985	Canada	ECHO	LV mass>215 gm ≥11.5 gm/m ²	74	51	66	LV mass ≥215 g, 56%, LV mass≥115 g/m ² , 71%
7	Klein RC et al., [9]	R	44	1984	USA	ECHO	LV mass>260gms	NA	NA	NA	47.70%
8	Komsuoglu B et al., [10]	R	70	1989	Turkey	ECHO	LV mass ≥215 gms	34	36	61	83%
9	Fragola PV et al., [7]	P	100	1990	Italy	ECHO	LV mass >241 gm >120 gm/m ²	58	42	39±14	66%
10	Mehta A et al., [11]	R	220	2000	USA	ECHO	Lvmass>215(W)>225(M)	154	66	65+-13	In LAE +LBBB group 92% had LVH
11	Rodriguez-Padial L et al., [4]	R	233	2012	Spain	ECHO	LV mass >134 gm/m ² >110 gm/m ²	124	109	67.1±12.6	60 .5%
12	Baronowski R et al., [6]	R	36	2012	Poland	MRI [†]	MRI	21	15	56	47%
13	Tavares CAM et al., [17]	R	68	2021	Brazil	ECHO	>95 gm/m ² (W)>115 g/m ² (M)	30	38	78.4	67.60%
14	DeBauge A et al., [12]	R	413	2023	USA	ECHO	>95 g/m ² (W)>115 g/m ² (M) RWT, >0.42, Concentric LVH <0.42, excentric LVH	194	219	74	37% (LV mass index)
15	DeBauge A et al., [13]	R	413	2024	USA	ECHO	>95 g/m ² (W)>115 g/m ² (M) RWT>.042, Concentric LVH<0.42, excentric LVH	194	219	74	37% (LV mass index)

[Table/Fig-3]: Baseline characteristics of included studies in the systematic review and meta-analysis. Study design, sample sizes, publication years, reference standards used, LVH diagnostic criteria, demographic data, and prevalence of LVH across 15 included studies spanning 1969-2024 [1,3-13,15-17].

R: Retrospective study; P: Prospective study; ECHO: Echocardiography; MRI: Magnetic resonance imaging; LV: Left ventricular; LBBB: Left bundle branch block; LAE: Left atrial enlargement; LAXD: Left axis deviation; Values are represented as mean±standard deviation, count and percentage

one study [17] assessing a predominantly elderly population (mean age 78.4 years).

The criteria were stratified into groups based on sample size >400, 300-400, and 200-300 patients and tabulated to show pooled sensitivity, specificity, LR+, LR-, DOR, PPV, NPV, and predictive accuracy. Because of the small patient representation, criteria with sample sizes <200 were not tabulated.

Results by Criterion Group

Criteria with sample size >400 [Table/Fig-4,5]: Among the parameters representing more than 400 patients, the Peguero-Lo Presti criterion had the highest pooled sensitivity of 0.878 but a low pooled specificity of 0.193. The Cornell VDP criterion had a pooled sensitivity of 0.757 and a specificity of 0.381. The Klein

criterion demonstrated the highest specificity (0.97) but had a sensitivity of only 0.136. Parameters with both sensitivity and specificity above 0.50 were QRS duration >160 ms, LAE, Cornell Voltage, SV2+SV3 >60 mm, and QRS duration >150 ms.

Criteria with sample size 300-400 [Table/Fig-6,7]: Among the parameters representing 300-400 patients, the Dalfo criterion had the highest pooled sensitivity (0.755), while max RV5 or V6 >25 mm demonstrated the highest pooled specificity (0.974).

Criteria with sample size 200-300 [Table/Fig-8,9]: Among the parameters representing 200-300 patients, the Kafka criterion demonstrated the highest sensitivity (0.75) and a specificity of 0.6366, and was the only criterion in this group with both sensitivity and specificity greater than 0.50. The remaining criteria in this group

S. No.	Criteria	Number of studies	Sample size (n)	Sensitivity	Specificity	Pooled prevalence	LR+	LR-	DOR	DOR 95% CI Lower Upper	
1	Sokolow-Lyon	12	1446	0.375	0.793	0.636	1.81	0.79	2.30	1.63	3.24
2	RaVL>11 mm	8	1109	0.187	0.929	0.636	2.64	0.87	3.02	1.84	4.96
3	Lewis index	5	691	0.249	0.879	0.636	2.06	0.86	2.39	1.36	4.20
4	Klein	2	513	0.136	0.970	0.636	4.55	0.89	5.09	2.31	11.20
5	QRS D>160 ms	5	711	0.601	0.653	0.636	1.73	0.60	2.86	1.88	4.36
6	LAE	7	625	0.523	0.903	0.636	5.39	0.53	10.20	5.82	17.87
7	Romhilt	3	401	0.442	0.805	0.636	2.26	0.69	3.26	1.87	5.70
8	Gubnierz	8	1075	0.202	0.891	0.636	1.86	0.89	2.09	1.28	3.42
9	LAD≥-30 degree	5	482	0.398	0.592	0.636	0.97	1.03	0.94	0.58	1.53
10	Max R+S(V1-V6)>45	3	608	0.403	0.845	0.636	2.59	0.71	3.64	1.82	7.29
11	Cornell Voltage	4	814	0.604	0.515	0.636	1.25	0.76	1.65	1.10	2.46
12	RV6/RV5>1	3	458	0.596	0.298	0.636	0.85	1.35	0.63	0.42	0.96
13	Sokolow-Lyon VDP ^{††}	3	714	0.424	0.680	0.636	1.33	0.84	1.57	1.03	2.41
14	Cornell VDP	3	714	0.757	0.381	0.636	1.22	0.64	1.90	1.22	2.95
15	RaVL VDP	3	714	0.458	0.707	0.636	1.56	0.76	2.06	1.34	3.17
16	SV2+SV3>60 mm	2	449	0.525	0.895	0.636	5.10	0.53	9.67	4.74	19.71
17	Peguero-Lo Presti	2	481	0.878	0.193	0.636	1.09	0.63	1.73	1.07	2.77
18	QRS D>150 ms	2	450	0.632	0.640	0.636	1.76	0.58	3.03	1.88	4.90
19	R1+SII≥26 mm	1	413	0.000	1.000	0.636	0.00	1.00	0.00	NA	NA

[Table/Fig-4]: Diagnostic accuracy measures for electrocardiographic criteria with representation of sample size >400 patients. Pooled sensitivity, specificity, likelihood ratios, DOR with 95% confidence intervals for ECG criteria.

LR+: Positive likelihood ratio; LR-: Negative likelihood ratio; DOR: Diagnostic odds ratio; PPV: Positive predictive value; NPV: Negative predictive value; CI: Confidence interval; LAE: Left atrial enlargement; QRS D: QRS duration; VDP: Voltage-duration product

S. No.	Criteria	PPV	NPV	Predictive Accuracy
1	Sokolow-Lyon	0.76	0.42	0.53
2	RaVL>11 mm	0.85	0.38	0.55
3	Lewis index	0.81	0.41	0.53
4	Klein	0.93	0.37	0.56
5	QRS D>160 ms	0.71	0.38	0.61
6	LAE	0.90	0.46	0.67
7	Romhilt	0.74	0.37	0.57
8	Gubnierz	0.81	0.40	0.53
9	LAD≥ -30 degree	0.67	0.43	0.48
10	Max R+S(V1-V6)>45	0.76	0.40	0.58
11	Cornell Voltage	0.62	0.38	0.52
12	RV6/RV5>1	0.56	0.34	0.41
13	Sokolow-Lyon VDP	0.67	0.38	0.53
14	Cornell VDP	0.64	0.50	0.58
15	RaVL VDP	0.70	0.40	0.55
16	SV2+SV3>60 mm	0.89	0.46	0.67
17	Peguero-Lo Presti	0.59	0.51	0.55
18	QRS D>150 ms	0.72	0.43	0.61
19	R1+SII≥26 mm	0.00	0.36	0.36

[Table/Fig-5]: Diagnostic accuracy measures for electrocardiographic criteria with representation of sample size >400 patients. Predictive values and Predictive accuracy for ECG criteria.

RaVL: R-wave amplitude in lead aVL; PPV: Positive predictive value; NPV: Negative predictive value; CI: Confidence interval; LAE: Left atrial enlargement; QRS D: QRS duration; VDP: Voltage-duration product

exhibited lower sensitivity (ranging from 0.85 to 0.58), although specificities ranged from 0.72 to 0.946.

The remaining 33 criteria, having sample sizes <200 patients, were not tabulated. Forest plots of sensitivity and specificity are depicted in [Table/Fig-10].

Analysis of DOR, Likelihood Ratios, and Predictive Accuracy:

Among the criteria with representation of more than 400 patients, the highest DOR was observed for LAE, which had a value of 10.2. LAE also demonstrated the highest positive LR (5.39). The lowest negative LR was reported for LAE and SV2+SV3>60 mm, both having a value of 0.53.

The highest PPV (0.93) was achieved using the Klein criterion, and the highest NPV (0.51) was observed for the Peguero-Lo Presti criterion.

Predictive accuracy greater than 0.6 was demonstrated by LAE, SV2+SV3>60 mm, QRS duration>160 ms, and QRS duration >150 ms, with LAE and SV2+SV3>60 mm being the highest (0.67). Twelve criteria demonstrated predictive accuracy between 0.5 and 0.6: Sokolow-Lyon, RaVL>11 mm, Lewis Index, Klein, Romhilt, Gubnierz, Max R+S (V1-V6)>45, Cornell Voltage, Sokolow-Lyon VDP, Cornell VDP, RaVL VDP, and Peguero-Lo Presti. The remaining criteria in this group (>400 patients) had very low predictive accuracy (<0.4).

SROC Curve Analysis

The SROC plot depicted in [Table/Fig-11] displays sensitivity versus (1-specificity) for all criteria without connecting line segments. Unconnected circles denote operating points for individual criteria,

S. No.	Criteria	Number of studies	Sample size	Pooled Sensitivity	Pooled Specificity	Pooled Prevalence	LR+	LR-	DOR	DOR 95% CI Lower Upper	
1	Max RV5 or RV6>25 mm	5	393	0.122	0.974	0.636	4.68	0.9	5.2	2.15	12.6
2	Dalfo	2	301	0.755	0.794	0.636	3.67	0.31	12.04	6.5	22.27

[Table/Fig-6]: Diagnostic accuracy measures for electrocardiographic criteria with representation of sample size 300-400 patients. Pooled sensitivity, specificity, likelihood ratios, DOR with 95% confidence intervals for ECG criteria.

LR+: Positive likelihood ratio; LR-: Negative likelihood ratio; DOR: Diagnostic odds ratio

S. No.	Criteria	PPV	NPV	Predictive Accuracy
1	Max RV5 or RV6>25 mm	0.95	0.36	0.62
2	Dalfo	0.85	0.49	0.73

[Table/Fig-7]: Diagnostic accuracy measures for electrocardiographic criteria with representation of sample size 300-400 patients. Predictive values and Predictive accuracy for ECG criteria.
PPV: Positive predictive value; NPV: Negative predictive value

S.No	Criteria	Number of studies	Sample size	Pooled Sensitivity	Pooled Specificity	Pooled Prevalence	LR+	LR-	DOR	DOR 95% CI Lower Upper
1	Kafka	2	225	0.75	0.636	0.636	2.06	0.39	5.31	2.7 10.45
2	Max R+S in V1-V6>45	3	268	0.532	0.74	0.636	2.05	0.64	3.22	1.73 5.98
3	RaVL>13	1	220	0.1	0.72	0.636	0.36	1.25	0.29	0.14 0.58
4	QRS D>155	2	257	0.58	0.77	0.636	2.52	0.55	4.56	2.3 9.05
5	Gubnierz VDP	1	233	0.177	0.946	0.636	3.26	0.87	3.74	1.28 10.92
6	12-Lead QRS VDP	1	233	0.298	0.913	0.636	3.41	0.77	4.43	1.72 11.41
7	SV1≥30	3	204	0.273	0.937	0.636	4.31	0.77	5.62	2.17 14.56
8	12 total QRS mv	1	233	0.106	0.967	0.636	3.22	0.92	3.5	1.01 12.18
9	Perugia	1	233	0.397	0.837	0.636	2.43	0.72	3.38	1.57 7.29
10	Romhilt estes	1	233	0.085	0.935	0.636	1.29	0.99	1.3	0.48 3.52

[Table/Fig-8]: Diagnostic accuracy measures for electrocardiographic criteria with representation of sample size 200 - 300 patients. Pooled sensitivity, specificity, likelihood ratios, DOR with 95% confidence intervals for ECG criteria.
LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, DOR: Diagnostic odds ratio; CI: Confidence interval; LAE: Left atrial enlargement; QRS D: QRS duration; VDP: Voltage-duration product

S. No.	Criteria	PPV	NPV	Predictive Accuracy
1	Kafka	0.75	0.41	0.64
2	Max R+S in V1-V6>45	0.72	0.42	0.6
3	RaVL >13	0.6	0.37	0.44
4	QRS D >155	0.76	0.43	0.62
5	Gubnierz VDP	0.82	0.38	0.56
6	12-Lead QRS VDP	0.85	0.4	0.59
7	SV1≥30	0.88	0.39	0.61
8	12 total QRS mv	0.9	0.38	0.58
9	Perugia	0.79	0.4	0.58
10	Romhilt estes	0.6	0.36	0.44

S. No.	Criteria	PPV	NPV	Predictive Accuracy
1	Kafka	0.75	0.41	0.64
2	Max R+S in V1-V6>45	0.72	0.42	0.6
3	RaVL >13	0.6	0.37	0.44
4	QRS D >155	0.76	0.43	0.62
5	Gubnierz VDP	0.82	0.38	0.56
6	12-Lead QRS VDP	0.85	0.4	0.59
7	SV1≥30	0.88	0.39	0.61
8	12 total QRS mv	0.9	0.38	0.58
9	Perugia	0.79	0.4	0.58
10	Romhilt estes	0.6	0.36	0.44

[Table/Fig-9]: Diagnostic accuracy measures for electrocardiographic criteria with representation of sample size 200-300 patients. Predictive values and Predictive accuracy for ECG criteria.
PPV: Positive predictive value; NPV: Negative predictive value; RaVL: R-wave amplitude in lead aVL (augmented vector left); QRS D: QRS duration; VDP: Voltage-duration product; SV1: S-wave amplitude in lead V1

and the dashed diagonal represents a non-informative classifier. Criteria positioned closer to the upper left indicate superior accuracy. The summary AUC was 0.42, indicating poor aggregate discriminative capacity.

Decision Curve Analysis and Clinical Utility

Decision curve analysis was performed for the 19 criteria with more than 400 patients. The decision curve analysis graph is shown in [Table/Fig-12]. The “treat-all” strategy demonstrated a greater net benefit than all individual ECG criteria. Thus, decision curve analysis within a threshold probability range of 0-50% failed to demonstrate clinical utility for any ECG criteria.

Risk of Bias Assessment of the Included Studies

The risk of bias across all four domains for the 15 included studies is shown in [Table/Fig-13]. The majority of studies demonstrated a low risk of bias across all domains. The patient selection and reference standard domains exhibited the highest methodological quality ($\geq 80\%$ rated low risk). The flow and timing domain showed the greatest uncertainty, reflecting incomplete reporting of test intervals or verification methods. No domain showed a substantial proportion of high-risk studies. These findings indicate that the

overall methodological quality of the evidence base is strong, and the diagnostic accuracy estimates derived from these studies can be interpreted with confidence.

Publication Bias Analysis

Publication bias was assessed across the included diagnostic accuracy studies using Deeks' asymmetry test. The slope coefficient from Deeks' regression test was not statistically significant ($p=0.788$),

suggesting that there was no strong evidence of small-study effects or publication bias among the included studies. However, the power to detect publication bias was limited due to the relatively small number of included studies ($n=15$). Therefore, while no significant bias was observed, the possibility of undetected bias cannot be fully excluded.

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Smaller studies did not disproportionately influence the pooled diagnostic estimates, as the funnel plot appeared symmetrical. Although a few included studies had small sample sizes (<50 patients), their results were consistent with those of larger studies, reinforcing the stability of the pooled findings. Overall, no evidence of publication bias was detected, and the diagnostic accuracy estimates for ECG-based LVH criteria can be considered methodologically reliable and unbiased.

DISCUSSION

LVH is commonly present in LBBB [4,5]; therefore, its diagnosis is crucial. ECG, being a widely used non-invasive tool for diagnosis [17], was evaluated in this meta-analysis to assess the efficacy of various ECG criteria in accurately diagnosing LVH in LBBB patients. However, no ECG criterion demonstrated adequate diagnostic accuracy.

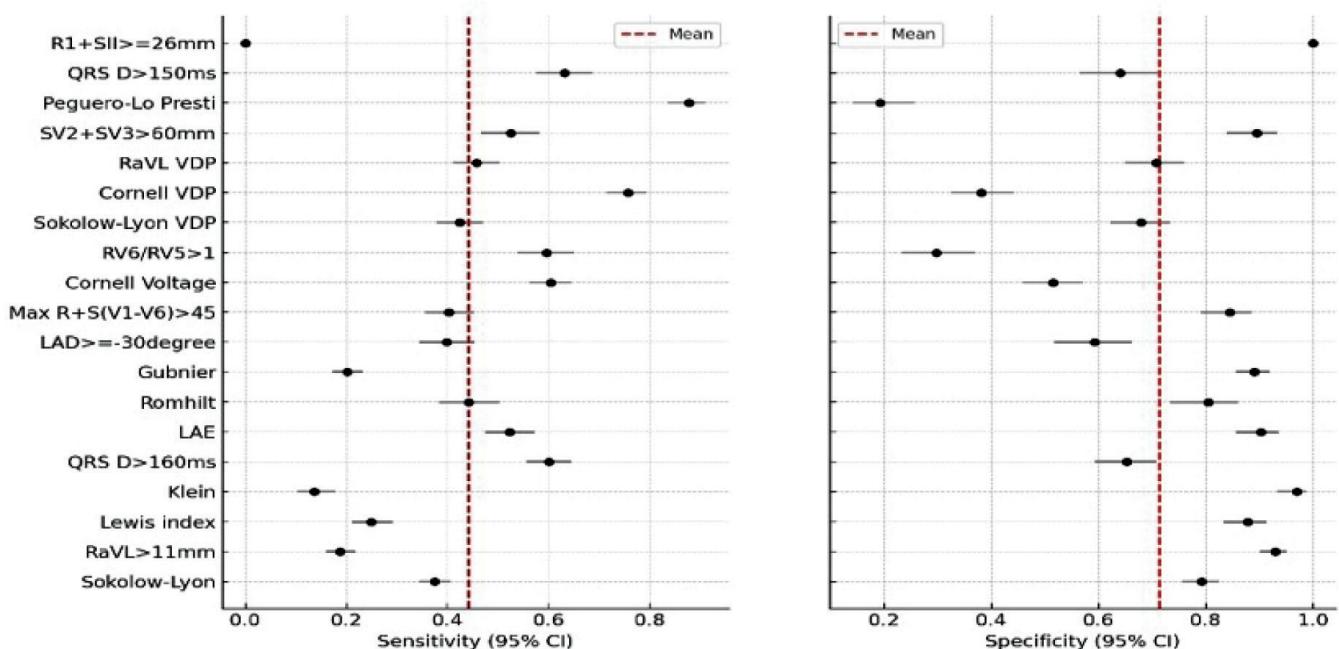
This meta-analysis demonstrated poor sensitivity and relatively high specificity for most ECG criteria used to diagnose LVH in LBBB patients, consistent with the observations of Tavares CAM et al., [17] and de Souza IAF et al., [18].

The low sensitivity observed for ECG criteria indicates that they are not effective in accurately detecting true positive cases of LVH in LBBB patients and therefore have poor clinical value. This finding correlated with the observations of Havelda CJ et al., [1].

Only two ECG criteria-Peguero-Lo Presti and Cornell VDP-showed sensitivities above 0.70 but demonstrated low specificities, limiting their accuracy in diagnosing LVH in LBBB patients. This finding was consistent with the observations of Tavares CAM et al., [17].

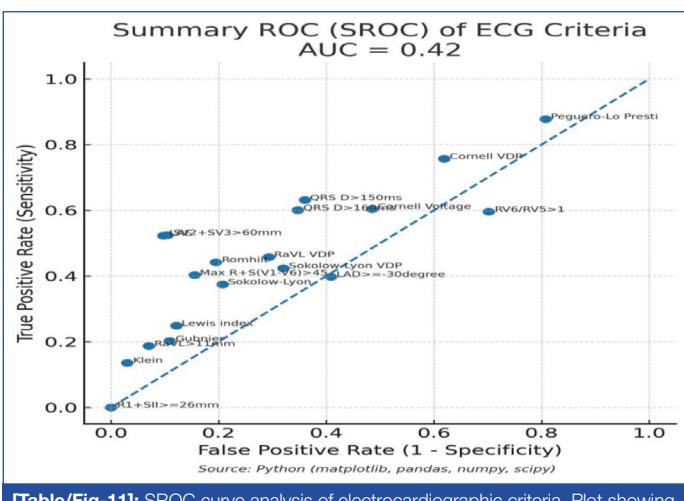
Klein criteria demonstrated the highest specificity, aligning with the findings of Fragola PV et al., [7]. However, none of the criteria

Forest Plots of Sensitivity and Specificity by ECG Criteria



Source: Python (matplotlib, pandas, numpy, scipy, statsmodels)

[Table/Fig-10]: Forest plots displaying sensitivity and specificity estimates for electrocardiographic criteria. Point estimates with 95% Wilson confidence intervals for individual ECG criteria, showing heterogeneity across studies and pooled effect measures for diagnostic accuracy meta-analysis.



[Table/Fig-11]: SROC curve analysis of electrocardiographic criteria. Plot showing sensitivity versus (1-specificity) for all evaluated criteria with area under curve calculation, demonstrating overall discriminative capacity for LVH diagnosis in LBBB patients.

showed a balanced trade-off between sensitivity and specificity, resulting in poor clinical utility. This observation agreed with those of Tavares CAM et al., [17] and de Souza IAF et al., [18].

Given the high pre-test probability of LVH in LBBB, ECG criteria with low negative likelihood ratios are required to exclude LVH effectively [17]. However, the likelihood ratios were inadequate for all ECG criteria in this meta-analysis, consistent with the observations of Tavares CAM et al., [17] and de Souza IAF et al., [18].

The lowest negative likelihood ratio was 0.53, achieved by the LAE and SV2+SV3>60 mm criteria, which was not sufficiently low to reliably rule out LVH in LBBB patients. This also correlated with previous findings [17,18].

The highest positive likelihood ratio was 5.39 (LAE criterion), which was still inadequate to confidently rule in LVH in LBBB patients. As such, due to insufficient likelihood ratios, ECG criteria cannot confidently rule in or rule out LVH and therefore indicate the need for additional imaging tests to confirm the diagnosis. This was consistent with the observations of Tavares CAM et al., [17] and de Souza IAF et al., [18].

This meta-analysis could not demonstrate adequate DOR for any ECG criteria. A DOR >10 was achieved by only one criterion (LAE), but the wide confidence interval limited its precision. Inadequate DOR values for all ECG criteria indicate poor discriminative ability to differentiate between LBBB patients with and without LVH, thereby limiting their clinical utility. These findings were consistent with those of de Souza IAF et al., [18].

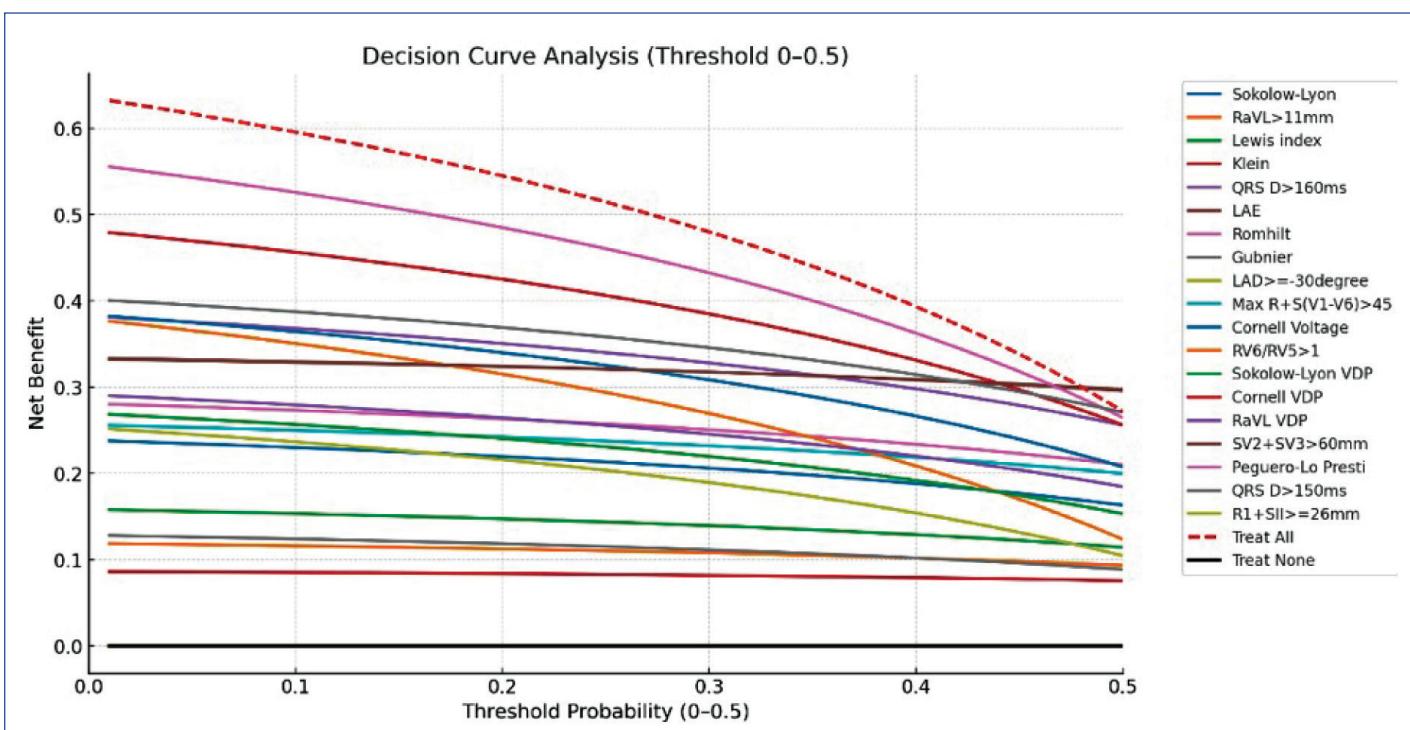
Given the pooled prevalence of LVH of 63.6% in the meta-analysis, it was found that none of the negative predictive values exceeded 51%. The poor negative predictive value, despite the high prevalence of LVH, makes all the criteria unreliable for ruling out LVH in LBBB patients, thereby limiting their diagnostic accuracy. A low NPV results in a higher incidence of false-negative diagnoses of LVH. This finding correlates with the observations of Havelda CJ et al., [1], Tavares CAM et al., [17], and de Souza IAF et al., [18].

In the meta-analysis, the predictive values were also inadequate for most ECG criteria, rendering them unreliable for confidently diagnosing LVH in LBBB patients. This correlated with the observations of Tavares CAM et al., [17] and de Souza IAF et al., [18].

It was observed that the highest predictive accuracy was only 0.67, and this was achieved by only two criteria, namely LAE and SV2+V3>60 mm. Overall, none of the ECG criteria demonstrated adequate accuracy for diagnosing LVH in LBBB patients. These findings correlated with the observations of Fragola PV et al., [7] and Havelda CJ et al., [1].

Among all the criteria, LAE had the highest DOR, the lowest negative likelihood ratio, the highest positive likelihood ratio, and the highest predictive accuracy, consistent with the findings of Noble LM et al., [15] and Mehta A et al., [11]. This also aligns with the view of Leo Schamroth, who stated that LAE is a useful sign to diagnose LVH in the presence of LBBB [19]. However, even this criterion demonstrated suboptimal diagnostic accuracy, and decision curve analysis failed to demonstrate its clinical utility.

The SROC curve analysis showed a pooled AUC of only 0.42. This indicates poor overall diagnostic accuracy for all the ECG indices and poor discriminatory power for distinguishing between LBBB patients with and without LVH. Therefore, ECG criteria cannot be solely relied upon by clinicians to rule in or rule out LVH in LBBB patients, necessitating further imaging modalities for confident diagnosis.



[Table/Fig-12]: Decision curve analysis evaluating clinical utility of electrocardiographic criteria. Net benefit curves across threshold probabilities (0-50%) comparing ECG-based diagnostic strategies with treat-all and treat-none approaches for clinical decision-making in LBBB patients.

S. no.	Study (Author, Year)	Patient selection	Index test	Reference standard	Flow and timing	Overall risk	Applicability concerns
1	Peterson GV et al., 1971 [8]	Moderate	Low	Low	Moderate	Moderate	Low
2	Zmyslinski RW et al., 1980 [5]	Low	Low	Low	Moderate	Moderate	Low
3	Havelda CJ et al., 1982 [1]	Low	Moderate	Low	Moderate	Moderate	Low
4	Noble LM et al., 1984 [15]	Low	Low	Low	Low	Moderate	Low
5	Haskell RJ et al., 1987 [16]	Low	Moderate	Low	Low	Moderate	Low
6	Kafka H et al., 1985 [3]	Low	Low	Low	Moderate	Moderate	Low
7	Klein RC et al., 1984 [9]	Low	Low	Low	Moderate	Moderate	Low
8	Komsuoglu B et al., 1989 [10]	Low	Low	Low	Moderate	Moderate	Low
9	Fragola PV et al., 1990 [7]	Low	Low	Low	Low	Low	Low
10	Mehta A et al., 2000 [11]	Low	Low	Low	Moderate	Moderate	Low
11	Rodriguez-Padial L et al., 2012 [4]	Low	Low	Low	Low	Low	Low
12	Baronowski R et al., 2012 [6]	Low	Low	Low	Low	Low	Low
13	Tavares CAM et al., 2021 [17]	Low	Low	Low	Low	Low	Low
14	DeBauge A et al., 2023 [12]	Low	Low	Low	Low	Low	Low
15	DeBauge A et al., 2024 [13]	Low	Low	Low	Low	Low	Low

[Table/Fig-13]: The risk of bias across all four domains for the 15 included diagnostic accuracy studies [1,3-13,15-17].

These results, showing a poor AUC, correlated with the observations of Tavares CAM et al., [17] and de Souza IAF et al., [18].

Decision curve analysis demonstrated that the net benefit of a Treat-all strategy was higher than that of any ECG criterion. This implies poor clinical benefit for all ECG criteria. Assuming LVH is present in all patients with LBBB, a strategy of performing additional imaging on every patient to diagnose LVH would be superior to relying on ECG criteria alone. Therefore, ECG should not be used as the sole diagnostic tool in clinical practice. This conclusion aligns with those of Fragola PV et al., [7], Tavares CAM et al., [17], and the meta-analysis by de Souza IAF et al., [18].

Due to inadequate balance between sensitivity and specificity, insufficient likelihood ratios and predictive values, poor AUC scores, and poor clinical utility demonstrated by decision curve analysis, none of the ECG criteria showed significant diagnostic accuracy for LVH in LBBB patients. These findings should be of value to clinicians managing patients with LBBB.

To overcome the above limitations, other imaging modalities such as echocardiography and cardiac MRI have emerged as valuable

tools for effectively diagnosing LVH in LBBB patients in conjunction with electrocardiography.

Limitation(s)

Our analysis had several limitations. First, the included studies displayed heterogeneity in design and populations across various geographical regions, used different gold standards for LVH, employed different LVH criteria, and utilised different ECG machine models, including older and newer computerised systems. Furthermore, the findings are based on a single dataset of diagnostic accuracy criteria rather than multiple independent datasets; therefore, external validation is warranted. Confidence intervals reflect sample size and variability, and wide intervals limit precision. Decision curve analysis assumes stable threshold-related preferences that may vary across clinical contexts.

CONCLUSION(S)

None of the ECG criteria demonstrated significant accuracy in diagnosing LVH in patients with complete LBBB. ECG should therefore not be used in isolation; additional imaging modalities

are essential for accurate diagnosis. Future studies utilising newer ECG parameters and artificial intelligence-based interpretation may improve diagnostic accuracy.

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