Automatic Diagnosis of Strict Left Bundle Branch Block from Standard 12-lead Electrocardiogram

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Abstract

Strict Left Bundle Branch Block (LBBB) criteria were recently proposed to identify patients with complete LBBB to benefit most from Cardiac Resynchronization Therapy (CRT). The objective of our study was to automate this strict LBBB criteria in order to facilitate broader application of the criteria which require the measurements of subtle QRS patterns from standard 12-lead ECGs. We developed a series of algorithms to automatically detect and measure the QRS parameters required for strict LBBB criteria. A total of 612 signal-averaged 12-lead ECGs from 612 LBBB patients were used to train and validate the algorithms. Four clinicians independently performed adjudication on equally assigned ECGs to assess the performance of automatic results comparing to manually adjudicated results, as well as the inter-observer and intra-observer variabilities.

Overall 95% and 86% of sensitivity and specificity are reached for detecting complete LBBB. Our study shows good performance in reference to manual results.

1. Introduction

Several analyses of clinical trials showed that patients with LBBB derived substantial clinical benefit from CRT, and no or little clinical benefit was observed in patients with a non-LBBB QRS pattern (right bundle-branch block or nonspecific LV conduction delay: intraventricular conduction disturbances) [1-3]. Approximately one third of patients diagnosed with LBBB by conventional electrocardiographic (ECG) criteria may not have complete LBBB [4]. In 2011, Strauss et al [5] proposed a new set of criteria to define complete “strict” LBBB which include QRS duration ≥ 140 ms (men) or ≥ 130 ms (women), QS or rS in leads V1 and V2, and mid-QRS notching or slurring in ≥ 2 of leads V1, V2, V5, V6, I, and aVL. Although the new strict LBBB criteria refine the detection of complete block of the left ventricular conduction system and provide insight into patient selection for CRT therapy, its validation and clinical utilities have not been evaluated in a larger cohort of patients. A computerized program with implementation of the criteria will enable its effective deployment in large database and clinical practice. In this work, we propose a novel computer program to automatically measure and detect complete LBBB based on the strict LBBB criteria.

2. Methods

2.1. Study population

This study involved the ECG recordings from patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial – CRT (MADIT-CRT) [6]. A set of 612 ECGs recorded prior to implantation were used from 612 patients with LBBB based on MADIT-CRT LBBB criteria (WHO criteria). Twenty ECGs were randomly selected for a training dataset. Four clinicians (ACR, MHR, NU and BS) independently reviewed and adjudicated automatic measurements, including 148 different ECGs assigned to each observer, along with 13 and 32 duplicated ECGs for evaluation of intra-observer variability and inter-observer variation respectively. Overall 185 ECGs were measured by each observer.

2.2. ECG recordings and signal averaging

12-lead high-resolution Holter ECGs were recorded before implantation using Mortara H12+ (Milwaukee, WI). The sampling frequency of the signal is 1000 Hz and the amplitude resolution is 3.75 μV.

The ECG signals used in this study were signal-averaged single beat tracings with standard 12-lead configuration (detail in [7]). The signal averaging process was performed on the first 20 minutes of Holter recording when the patients were resting in supine position. A minimum of 130 sinus beats were required for the signal averaging process.

2.3. Strict LBBB detection

QRS duration

A QRS detector was implemented based on a linear transformation algorithm developed by Zong et al. [8]. Some modifications were made to the algorithm to improve the location of boundaries for wider QRS duration in LBBB patients, i.e. ranging from 130ms to 200ms (Figure 1A). These adjustments include: the elimination of the adaptive threshold procedure required for multiple beats signal, and an adjustment of the detection thresholds of the onset and offset of the QRS complex [7].

Characterization of QRS morphology

The QRS morphology is characterized based on conventional nomenclature which defines each positive or negative deflection reference to the isoelectric (IE) line (Figure 1B). To determine the QRS shape, we implemented a method identifying signal transitions and using the transition points and their polarity to fit the QRS patterns (details see [7]).

Notch and Slur detection

We applied notch and slur detection methods [7] to locate all notches and slurs in six consecutive leads (Figure 1C). Briefly, four core steps were involved: 1) the noise level in each lead was estimated using the standard deviation of signal with 20ms length before QRS onset. It was used to establish thresholds for notch detection and signal filtering in slur detection. 2) ECG signal inside QRS complex was traced to locate upward and downward segment. Fragmentation is detected when a segment does not cross over the IE line and it is registered as a notch. 3) Peak and nadir detection method combining with noise-adaptive threshold were used to find all peaks and nadirs. Criteria based on geometrical properties (height, width and area) of notch were applied to select true notches. 4) Slur detection was performed on each segment following noise-adaptive filtering [7].

Procedures for diagnosis of strict LBBB

Presence of mid-QRS notching or slurring was determined by the position of notch/slur which should begin after the first 40ms and before 50% of QRS duration, also end before 2/3rd of the QRS duration. Finally the decision rules of true LBBB are based on global QRS duration, QRS morphology in leads V1 and V2 and the number of consecutive leads with mid-QRS notching or slurring.

2.5. Measurement evaluation

Mean absolute deviation (MAD) was measured for assessing the intra- and inter-observer variabilities on continuous variables. MAD value is calculated as formula 2.1. $\bar{X}$ was the mean of measurements on same ECG, N was the number of observers/measurements.

$$MAD = \frac{\sum_{i=1}^{N}|X_i - \bar{X}|}{N} \qquad 2.1$$

The level of agreement for binary variables (presence /absence of notch or slur) was calculated as the ratio of the number of observers with similar findings (presence or absence of a notch/slur) to the total number of observers.

The sensitivity was computed as the percentage of correctly identified patterns by automatic method to the number of patterns detected manually, and the specificity was measured as the percentage of correctly identified negative patterns (non-existing) by automatic method to the number of negative patterns detected by manual.

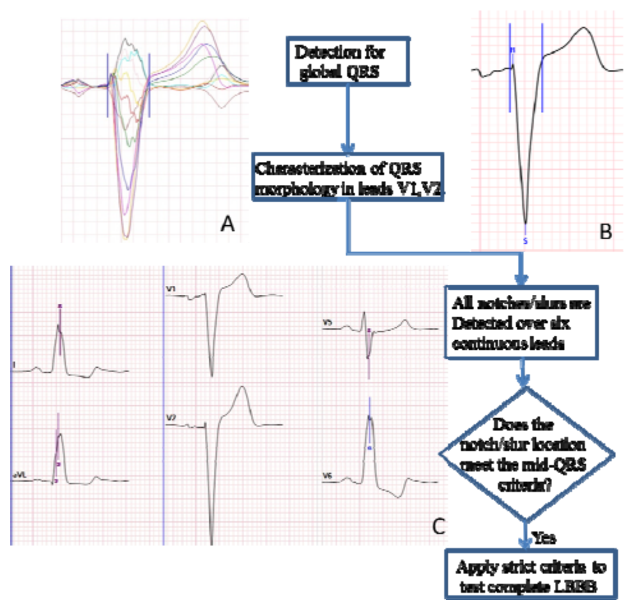

Figure 1. Schematic flow chart for detection of complete LBBB applying Strauss' strict criteria on 12-lead ECG. A) Define global QRS boundaries (two vertical blue bars). B) Characterization of QRS morphology in leads V1 and V2 (RS label in figure). C) Detection of all notches/slurs over six leads (notch: blue bar with label "n". slur: purple bar with label "s").

2.6. Statistical analysis

Student paired t-test was used to assess the difference between two measurements on the same subject. One-way repeated measures ANOVA analysis was performed for more than two measurements on the same subject. A p value < 0.05 was considered statistically significant.

3. Results

3.1. Continuous variables

The absolute differences on locating the beginning of QRS (QRS onset), the end of QRS (QRS offset) and QRS duration were all below 2ms for intra-observer, inter-observer and automatic vs manual adjudicated measurements (Table 1). None of these measurements were significant different for same observer, but significantly different among four observers and automatic vs manual (except locating QRS among four observers).

Lead V5 retains the largest difference on notch and slur locations for intra-observer, inter-observer and automatic vs manual measurements. The smallest difference on locating notch was found in lead I for both intra- and inter-observer. However, the leads with smallest difference on slur locations are V6 and V2 respectively. P-values show significant difference for locating slur on leads V1 and V5, and locating notch on lead V2 among four observers. On the other hand, the smallest differences on notch and slur locations for automatic vs manual measurements were observed in lead V1.

Table 1: The MAD results for continuous variables (unit: ms) measured for inter-observer, intra-observer and automatic vs. manual. The difference reaching significance ($p < 0.05$) is in bold.

	Inter-Observer	Intra-Observer	Auto vs. Manual
N (No. of ECGs)	31	13	583
QRS Duration	**1.4 ± 1.7**	1.5 ± 1.6	**0.9 ± 1.2**
QRS onset	0.6 ± 1.2	0.9 ± 1.0	**0.5 ± 0.5**
QRS offset	**1.4 ± 2.1**	1.7 ± 1.9	**0.5 ± 0.8**
Notch I	0.08 ± 0.23	0.15 ± 0.19	0.01 ± 0.02
aVL	0.21 ± 0.56	0.39 ± 0.47	0.04 ± 0.04
V1	0.11 ± 0.64	0.38 ± 0.51	0.00 ± 0.01
V2	**0.16 ± 0.66**	0.41 ± 0.54	0.00 ± 0.00
V5	0.41 ± 0.98	0.70 ± 0.84	0.05 ± 0.02
V6	0.26 ± 0.76	0.51 ± 0.63	0.02 ± 0.03
Slur I	0.68 ± 1.77	1.22 ± 1.5	0.09± 0.15
aVL	0.43 ± 1.59	1.01 ± 1.3	0.13 ± 0.22
V1	**0.38 ± 1.22**	0.80 ± 1.0	0.04 ± 0.08
V2	0.18 ± 0.99	0.58 ± 0.79	0.11 ± 0.19
V5	**0.95 ± 2.0**	1.47 ± 1.72	0.20 ± 0.35
V6	0.32 ± 0.99	0.45 ± 0.58	0.08 ± 0.12

3.2. Presence of notch/slur

Agreements on the presence and absence of notch over six consecutive leads range from 97% (V1) to 88% (aVL) within same observer, and from 98% (V1, V2) to 93% (I) among four observers. Meanwhile, the ranges of agreements on slur are from 97% (V2) to 83% (I), from 95% (V2) to 87% (I) respectively for intra- and inter-observer variabilities. The average agreements in six leads were presented in table 2.

The overall ability of the automatic algorithms to appropriately detect the presence and absence of all notch/slur inside QRS are reported in Table 2 in terms of sensitivities and specificities. The ranges of sensitivity and specificity for notch are 84% (V2)-89% (aVL) and 91% (aVL) -98% (V1, V2and V6) respectively; while ranges for slur are 75% (V2) - 82% (V6) and 86% (I)-93% (V2).

Table 2: Sensitivity and specificity of notch/slur using automatic method reference to manual adjudication detection are presented in the first two columns. Also, the agreement of the presence or absence for notch/slur among observers (inter-observer) and inside observer (intra-observer) is reported.

	Sensitivity (%) (Auto-Manual)	Specificity (%) (Auto-Manual)	Inter-Observer Agreement (%)	Intra-Observer Agreement (%)
Number of ECGs	148 X 4	148 X 4	31 (4 observers)	13 (4 observers)
Notch: I	86±11	94±5	93±11	95±12
aVL	89±10	91±8	94±15	88±32
V1	86±10	98±3	97±9	98±7
V2	84±9	98±2	97±11	94±17
V5	86±7	94±5	94±10	90±24
V6	88±9	98±2	94±11	94±15
Overall	87±9	96±4	95±11	93±18
Slur: I	76±16	86±14	87±15	83±36
aVL	77±17	92±12	89±21	90±19
V1	78±15	91±14	90±14	92±19
V2	75±17	93±12	95±12	97±11
V5	79±13	87±17	89±15	84±25
V6	82±14	88±14	91±14	84±23
Overall	78±15	90±14	90±15	88±22

3.3. True LBBB test results

We tested how well the automatic method detected the presence of mid-slur/notch comparing to manual measurements (Table 3). The sensitivity and specificity were 95% and 85%, respectively. Also, the sensitivity and specificity for testing complete LBBB applying strict criteria were 95% and 86%. The range of sensitivity for testing complete LBBB was from 87% to 98% however the range of specificity was much wider: 53% to 100%.

Observer	Sensitivity Slur/Notch(%)	Specificity Slur/Notch(%)	Sensitivity LBBB (%)	Specificity LBBB (%)
1	87	99	87	99.6
2	98	55	98	53
3	98	100	97	100
4	98	88	97	93
Overall	95±5	85±21	95±5	86±22

Table 3: The performance of automatic classification on the presence of mid-slur/notch and true LBBB.

4. Discussions

In addition to QRS duration and the leads V1 and V2 QRS morphology, Strauss's strict LBBB criteria accentuate the presence of mid-slur/notch in six consecutive leads. Currently, there is no standard definition of QRS notch and slur patterns, and clinicians usually have their own interpretation. We developed these definitions in collaboration with experts in the field [7] using a pattern recognition approach to detect the subtle changes within the QRS complex. In this study, we evaluated and compared the performance of automatic algorithm with manual measurements independently performed by 4 clinicians in 592 signal-averaged ECGs. Meanwhile, 13 and 32 ECGs were randomly selected for assessing intra-observer and inter-observer variability. The accuracy of slur/notch detection and location were assessed on both binary and continuous variables.

Automatic characterization of QRS morphology in leads V1 and V2 reached 100% accuracy. Also with average difference below 1ms, the precision of QRS duration was found to be satisfactory. To evaluate the performance of slur/notch detection, all slur/notch inside the QRS complex were measured and compared. Lead V5 has the highest MAD value for slur and notch location in all three comparison groups: automatic vs manual, intra-observer and inter-observer. This could link to the fact that the QRS morphology changes from rS to R around lead V5 location in the horizontal plane which resulted in relatively lower amplitude of R or RS wave. Not surprisingly, the lowest MAD value for slur/notch were mostly observed in leads V1 and V2 where the amplitude of QRS reached the highest and was less affected by noise. Generally, the measure of the time location of a slur was more challenging than that of notch because the slur patterns have larger time span and it is generally difficult to visually assess the boundaries of such patterns.

In this study, we developed a series of algorithms to automatically compute all measurements and decision rules for ECG based strict LBBB criteria. In the meantime, the algorithms and detection procedures are embedded into a software package that was designed with a user interface enabling simple review the automatic measurements and their manual adjustment when needed. More importantly, this method will be integrated into our newly developed QuAReSS software which automatically calculates QRS Selvester Score for patients meeting strict LBBB criteria [7] and therefore ensuring a fully automatic computation of the Selvester score without manual pre-selection of the tracings.

5. Conclusions

In this paper, we have proposed a computer based software for the automated detection of complete LBBB applying strict criteria. Our validation results show that the proposed automated system achieves approximately 95% accuracy which is equivalent to the level of inter-observer variability. With such level of accuracy, the proposed automated system could be potentially used to validate the strict criteria in large databases and further facilitate large-volume screening of patients eligible for implantation of CRT and improve their outcomes.

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