Late Potential Analysis: Is a Mathematically-Derived X, Y, Z Lead System Comparable to a True Orthogonal X, Y, Z Lead System?

Thomas A. Cron, Michael J. Zellweger, Peter T. Buser,
Matthias E. Pfisterer, and Stefan Osswald

From the Division of Cardiology, University Hospital, Basel, Switzerland

Background: Analysis of ventricular late potentials (LP) with signal-averaged ECG (SAECG) using three bipolar, orthogonal X, Y, Z leads is a validated method of risk-stratification in patients prone to ventricular tachycardia. The aim of this study was to validate a ECG system, which allows LP analysis using X, Y, Z leads mathematically derived from the standard 12-lead ECG.

Methods and Results: In 36 patients (age 56 ± 12 years, coronary artery disease 71%, LVEF $46 \pm 14\%$) with known or suspected ventricular tachyarrhythmia, two consecutive SAECGs were recorded, one with mathematically derived and another one with true X, Y, Z leads. Time domain measurements with these different lead systems were compared using linear regression analysis and "Bland-Altman" plots. Correlation was good ($r = 0.92$) for the filtered QRS complex duration, but poor for the terminal QRS amplitude (RMS) and duration (LAS) criteria ($r = 0.66$ and 0.61 , respectively; $P < 0.0001$). Defining LPS as present if at least two of the three time domain criteria were abnormal, the result matched in 28 (78%), but differed in 8 (22%) patients.

Conclusion: SAECG using X, Y, Z leads mathematically derived from the standard 12-lead ECG compared to true bipolar X, Y, Z leads show a close correlation in filtered QRS duration, but can differ considerably in the other time domain measurements, resulting in different interpretation of LP analysis in 22%. Therefore, SAECG registration should currently be performed with true X, Y, Z leads, until the accuracy of other approaches is validated.

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Analysis of ventricular late potentials (LP) using signal-averaged ECG (SAECG) is an established noninvasive method of risk stratification in patients prone to ventricular tachycardia, mainly after recent myocardial infarction.¹⁻³ Late potentials are low amplitude, high frequency signals in the terminal QRS complex originating from diseased myocardial tissue with slow conduction, which represents the arrhythmogenic substrate for ventricular arrhythmias.

According to international guidelines, most studies in time-domain analysis of SAECG have used a bipolar X, Y, Z lead system.^{4,5} Some commercially available ECG systems perform LP analysis using X, Y, Z leads mathematically derived from the standard 12-lead ECG. This approach is easy and time

saving, but its diagnostic and prognostic accuracy has never been demonstrated. Therefore, the aim of this study was to validate the accuracy of time domain measurements in SAECGs using X, Y, Z leads mathematically derived from the 12-lead ECG.

METHODS

This prospective study included 50 consecutive patients who were evaluated for ventricular arrhythmia using late potential analysis. In all patients, the same commercially available ECG system (Schiller Model AT 60, Software V 2.18; Schiller AG, Baar, Switzerland) was used. SAECG-registration was performed after usual skin prepa-

*Address for reprints: Thomas A. Cron, M.D., Division of Cardiology, University Hospital, Petersgraben 4, CH-4031 Basel, Switzerland.
Fax: +41-61-265 45 98; E-mail: tcron@uhbs.ch*

ration and using self-adhesive silver-silver chloride electrodes (Red Dot, 3M Health Care, Germany). According to the study design, two consecutive SAECG recordings were performed in each patient, one with standard 12-lead ECG positions (X,Y, Z leads mathematically calculated, see below) and another one with recording of bipolar, uncorrected orthogonal X,Y, Z leads (control). The true bipolar orthogonal leads represent horizontal (X), vertical (Y), and sagittal (Z) axes and were attached in the following positions: X- / X+: right/left mid axillary line, at the level of the fourth intercostal space; Y-: at the superior aspect of the manubrium sterni (jugulum), Y+: inferior end of the sternum (epigastrium); Z+: left sternal border, at the level of the fourth intercostal space (V2 position), Z-: posterior, left paravertebral, opposite to Z+. The X,Y, Z leads mathematically derived from the standard 12-lead ECG recording were calculated as follows: $X = 17/16 V1$, $Y = 9/16 (II + III)$, and $Z = (2 V6 - 25 V2)/54$. For signal averaging 300 beats were recorded, digitized at a sampling rate of 1000 Hz and a bandwidth of 0.05 Hz to 250 Hz. Ectopic or noisy beats were automatically excluded if correlation with the initial template beat was < 98%. Noise was kept below 1.0 μV . After filtering with a bidirectional Butterworth highpass filter at 40 Hz, the vector magnitude (V_i) was calculated using the formula $V_i = (x_i^2 + y_i^2 + z_i^2)^{1/2}$. Based on this vector magnitude (also called "filtered QRS complex") the late potential analysis was performed using standard time domain parameters. According to international standards, time domain analysis included three criteria with the following cut-offs for an abnormal (positive) test: 1) a duration of the filtered QRS complex (HF-QRSd) greater than 114 ms; 2) a terminal low amplitude signal (LAS) remaining below 40 μV for more than 38 ms; and 3) a root mean square voltage (RMS) during the last 40 ms of the filtered complex of less than 20 μV . Late potentials were defined as present (positive) if at least two of the three time domain criteria were abnormal.^{4,5}

Statistical analysis was performed with StatView (version 4.5, SAS Institute Inc., Cary, NC, USA). All three time domain parameters acquired with the two different lead systems were compared using linear regression analysis and "Bland-Altman" plots.⁶ Noise levels were compared with paired *t*-test. P values < 0.05 were considered statistically significant.

RESULTS

In 50 consecutive patients with a history or high suspicion of ventricular tachyarrhythmia, signal-averaged ECG was performed as described above. Fourteen patients had to be excluded from the study because of bundle branch block (*n* = 5), noise-level > 1.0 μV (*n* = 6), or obviously incorrect results of the automatic measurements of HF-QRSd (incorrect position of the markers for the beginning and end of the QRS complex, *n* = 3). The remaining 36 patients were included for further analysis. The patient characteristics of these patients are shown in Table 1. Eighteen (50%) patients had documented ventricular tachyarrhythmias; 7 (19%) patients had unexplained syncope (3 with documented nonsustained VTs); 8 (22%) patients had an implanted cardioverter defibrillator. In 14 (39%) patients, no ventricular tachyarrhythmia was documented.

Linear regression analysis of the duration of the filtered QRS complex (HF-QRSd), measured with true orthogonal X,Y, Z lead positions compared to the measurements mathematically derived from the standard 12-lead ECG, showed a good correlation (Fig. 1a). However, the other two time domain parameters, RMS voltage and LAS duration showed a somewhat poorer but still significant correlation (Fig. 1b,c). According to the method described by Bland and Altman,⁶ the difference of the two measurements were plotted against their average (Fig. 2a-c). For all three variables the differences were within the 95% limits of agreement (mean $\pm$ 2 SD). The mean differences are $+5.2 \pm 5.8$ ms for the filtered QRS duration, -3.1 ± 10.8 ms for the LAS duration, and $+8.0 \pm 14.3$ μV for the RMS-voltage. There is no obvious trend in

Table 1. Patient Characteristics (*n* = 36)

Age (years, mean $\pm$ SD)	56 $\pm$ 12
Females	5 (14%)
Diagnosis	
Coronary artery disease	26 (71%)
Other cardiopathy	3 (9%)
No structural heart disease	7 (20%)
Left ventricular ejection fraction (% $\pm$ SD)	46 $\pm$ 14
Arrhythmia history	
Ventricular fibrillation	3 (8%)
Sustained VT	4 (11%)
Nonsustained VT (NSVT)	11 (31%)
Syncope (8% with NSVT)	7 (19%)
None, unknown	14 (39%)

Figure 1. Linear regression analysis of three time domain parameters measured with true, orthogonal X,Y, Z leads compared to X,Y, Z leads mathematically derived from the standard 12-lead ECG: **(a)** HF-QRS-duration = duration of the filtered QRS-complex; **(b)** RMS voltage = root mean square voltage during the last 40 ms; **(c)** LAS duration = duration of the terminal low amplitude signal below 40 μV . In all three regression plots, x axis depicts values measured with the true X,Y, Z lead system, whereas y-axis depicts measurements with X,Y, Z leads mathematically derived from the standard 12-lead ECG.

the scatter of the differences for the filtered QRS duration (Fig. 2a) and LAS duration (Fig. 2c). On the other hand, the difference of mea-

sured RMS voltage seems to rise with increasing magnitude of the mean RMS voltage (positive slope of the regression line, Fig. 2b).

Figure 2. Differences (y-axis) are plotted against averages (x-axis) of the measured time domain parameters in SAECC recorded with the two different lead systems. (Solid lines = regression lines, broken lines = mean of differences, dotted lines = 95%-limits of agreement; shaded area marks pathologic values; abbreviations see Figure 1).

The results of the late potential analysis using true orthogonal X,Y, Z leads were positive (i.e., LPS were present) in 12 (33%) and negative in 24 (67%) patients. Analysis mathematically derived from the standard 12-lead ECG were positive in 16 (44%) and negative in 20 (56%) patients. Comparing the two different lead systems, the results matched in 28 (78%) and differed in 8 (22%) patients.

The mean noise level measured during the SAECG recordings with X,Y, Z leads mathematically derived from the standard 12-lead ECG was significantly lower than during the registrations using true orthogonal X,Y, Z leads ($0.3 \pm 0.1 \mu\text{V}$ vs. $0.6 \pm 0.3 \mu\text{V}$, $P < 0.001$). The noise levels in the subgroup of patients with matching results of the LP analysis in both lead systems ($n = 28$) were not significantly different from those patients with a result mismatch ($n = 8$).

DISCUSSION

The purpose of this study was to compare time domain measurements of SAECG recorded with two different lead systems in the same patient. Regression analysis of the results show a close correlation ($r = 0.92$) of the duration of the filtered QRS complex and a poorer correlation of the other two time domain criteria, RMS voltage ($r = 0.66$) and LAS duration ($r = 0.61$). The correlation coefficient (r) measures only the strength of correlation between the two measurements but not the agreement between them. Therefore, additional analyses using "Bland-Altman plots" were performed (Fig. 2a-c).⁶ The mean differences between the two methods of SAECG registration (HF-QRSd = $+5.2 \pm 5.8$ ms, LAS = -3.1 ± 10.8 ms, RMS = $+8.0 \pm 14.3 \mu\text{V}$) can be interpreted as the systematic bias of the two methods. RMS voltage measurements (Fig. 2b) show the greatest bias, with an additional increase in bias with rising RMS voltage magnitude. For all three measured variables, the differences were within the 95% limits of agreement, suggesting an acceptable fluctuation of the two methods. The question remains, whether these systematic biases and fluctuations within ± 2 SD are clinically acceptable. The interpretation of SAECG (i.e., late potentials present or not) relies on fixed cut-off values for the three time domain variables (see Methods). Figures 2b+c show that the scatter of the measured differences in RMS voltage and LAS duration clearly crosses the cut-off lines. Therefore, the agreement of RMS voltage and LAS

duration between the two methods is insufficient. Visual analysis of Figure 2a shows a more acceptable agreement for filtered QRS durations.

Many different factors in hardware or software algorithms used for SAECG recording, as well as changing patient or measurement conditions, are known to influence LP analysis. On the other hand, previous studies from different laboratories reported close correlation and reproducibility of time domain measurements from serial SAECG recordings in stable patient populations and with standardized settings for LP registration and analysis.⁷ Borbola and Denes tested the short-term reproducibility of SAECG recorded 1 hour apart and showed a very high correlation for the measurements of filtered QRS-, LAS duration, and for RMS voltage ($r = 0.98 - 0.99$).⁸ In our study, the two different SAECG recordings were performed immediately one after the other and no patient was in unstable condition. In addition, the same ECG system and unchanged, standardized settings for sampling and filtering were used in all patients. Therefore, the poor agreement of LAS duration and RMS voltage measurements is not explained by changing measurement conditions or lacking reproducibility.

Further, noise levels are known to affect the LP measurements. With both lead systems, very low noise levels were achieved, demonstrating a sufficient quality of the SAECG recordings (derived from 12-lead ECG = $0.3 \pm 0.1 \mu\text{V}$; true X,Y, Z leads = $0.6 \pm 0.3 \mu\text{V}$). Nevertheless, the difference of these noise levels is statistically significant ($P < 0.001$). The higher noise levels with true X,Y, Z leads could be caused by the fact that in this lead system only eight of the ten leads of a standard ECG are used for registration. The noise levels in the subgroups of patients with matching versus nonmatching LP analysis were consistent and therefore noise levels are not the explanation for an insufficient agreement between the two methods of SAECG registration.

Different lead placements have been used for SAECG.⁹ In recent years, most studies in time domain analysis of SAECG have been performed using true bipolar orthogonal X,Y, Z leads, recognized as gold-standard since 1991.⁴ Theoretically, X,Y, Z leads derived from the standard 12-lead ECG, would offer the advantage of LP analysis without additional recording with different lead positions. Performing LP analysis simultaneously with the conventional 12-lead ECG would be easy and time saving and therefore, could increase the acceptance of SAECG in routine cardiac diagnosis.

tics. More than a decade ago, it was shown that vectorcardiograms can be accurately obtained with orthogonal X,Y, Z leads mathematically derived from the 12-lead ECG.^{10,11} Theoretically, similar mathematical techniques should also work for SAECG, but to our knowledge, the accuracy of such software algorithms performing LP analysis with "virtual" X,Y, Z leads derived from the standard 12-lead ECG has not been investigated so far.

Comparing the two different lead systems and defining LP analysis positive (i.e., LP present) if two out of three criteria were abnormal, the results of the LP analysis did not match in 8 of 36 (22%) patients. If the results of the SAECG recorded with the true X,Y, Z lead positions were considered as the reference, LP analyses derived from standard 12-lead ECG were false positive in 6 and false negative in 2 patients, suggesting a higher sensitivity and lower specificity of the analysis derived from the 12-lead ECG. This discrepancy is mainly caused by different results of LAS and RMS measurements. Only in 4 patients, SAECG revealed a duration of the filtered QRS complex > 114 ms. In these 4 patients all three time domain criteria were abnormal in both measurements with either lead system (complete match).

LIMITATIONS

In spite of the discrepancies noted in LAS and RMS measurements, the number of patients included in this study is too small to prove or disprove the accuracy of the mathematic algorithm used to derive X,Y, Z leads from the standard 12-lead ECG. Furthermore, this study is limited to a comparison of the "numeric" results of time domain measurements in SAECG using two different lead systems. No clinical validation of the predictive value in risk stratification for ventricular arrhythmia was performed and therefore, no data or conclusions about the prognostic accuracy of either test can be made.

CONCLUSIONS

SAECG using X,Y, Z leads mathematically derived from the standard 12-lead ECG compared to true bipolar X,Y, Z leads show a close correlation in filtered QRS duration (HF-QRSd), but can differ considerably in LP amplitude and duration criteria (LAS, RMS), resulting in a different interpretation of LP analysis in up to 22% of the patients. Therefore, SAECG registration should currently be performed using true X,Y, Z leads only, until the diagnostic and prognostic accuracy of other approaches are properly validated in further studies.

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