Optimizing Risk Stratification: A Modified Signal-Averaged ECG Method

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Abstract

The signal-averaged ECG (SA-ECG) has established value in identifying patients a risk for serious ventricular arrhythmias following myocardial infarction. The standard SA-ECG has high negative (90-100%), but low positive (10-35%) predictive value. This latter characteristic appears, in part, related to the method by which the SA-ECG is derived. Given that the onset & offset of the QRS complex and the presence or absence of late potentials are inherently related to the signal to noise ratio, it may not be appropriate to derive these parameters using a single set of ECG epochs. To further address this issue, 78 individual SA-ECG recordings were analyzed at a target noise level of 0.5 μV and at a fixed number of templates (300). Using our modified approach, a significant percentage of patients were classified as "indeterminate" in that the confidence interval for QRS width crossed the threshold level.

1.   Introduction

Cardiac disease is the most common cause of natural death in the Western hemisphere and accounts for 40% of deaths in Canada each year [1, 2]. Approximately 50% of all cardiac deaths result from serious arrhythmias [1]. Individuals with ischemic heart disease, particularly those with a history of myocardial infarction (MI) represent a large proportion of those at risk of for sudden death [2-4]. In order to institute effective preventive therapies, such as the implantable cardioverter defibrillator, patients at risk for serious arrhythmias need to be accurately identified [5].

Signal averaged electrocardiography is a technique involving the averaging of hundreds of ECG waveforms to facilitate the analysis of microvolt signals, termed ventricular late potentials, which are part of the terminal portion of the QRS complex [6]. These late potentials represent areas of delayed and fragmented ventricular activation that occur after an acute myocardial infarction. Ventricular late potentials are usually not apparent on standard surface ECG signals because their voltages are too small in amplitude to be detected. However, the identification of these potentials is clinically important. Specifically, slow and inhomogeneous conduction propagation is an important condition for the occurrence of reentry, and most clinically significant ventricular arrhythmias in the setting of previous myocardial infarctions are reentrant in origin (Figure 1).
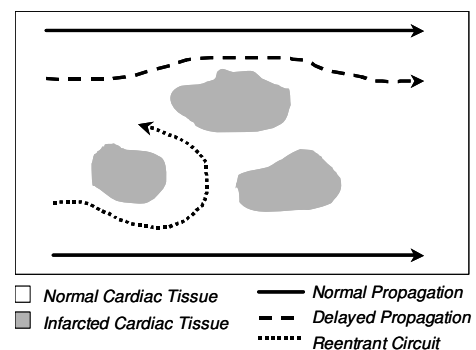

Figure 1: Schematic Illustration of delayed propagation and reentry phenomenon.

Ventricular late potentials are identified by marked QRS prolongation or low amplitude, high frequency waveforms in the terminal part of the QRS and initial part of the ST segment[7]. Therefore, SA-ECG QRS width provides prognostic information regarding the future risk of serious arrhythmias.

As stated above, ventricular late potentials are usually not apparent on standard surface ECG signals because their voltages are too small in amplitude to be detected. Hence, the purpose of signal averaging is to reduce the level of background noise and hence facilitate the analysis of these potentials. The noise sources are both intrinsic (e.g. skeletal muscle activity) and extrinsic (e.g. powerline interference, electrodes, amplifiers) to the body [8]. Under optimal conditions, the noise amplitude of the raw ECG signal is typically on the order of 5 to 20 μV.

The ECG signal can be averaged in two different ways: spatial and temporal. In terms of the former, potentials from a series of independent electrodes (typically four to 16) are averaged, yielding a theoretical noise reduction of $1/\sqrt{N}$ where N is the number of electrodes. The advantage of spatial averaging is that transient events can be examined [8]. However, there is a practical limit to the number of electrodes that can be employed, and this number may not be sufficient to

reduce the noise to a level at which the ventricular late potentials can be identified. In addition, closely spaced electrodes may record a common noise source which would not be effectively reduced by the averaging procedure [8].

In temporal averaging, sequential samples of a repetitive waveform are averaged. In this case, random noise is reduced in proportion to the square root of the number of ECG beats that are processed. In most studies, the averaging of 200 to 500 beats results in background noise levels less 1.0 μV. The advantage of temporal averaging is that only a signal electrode is required. However, in using this form of averaging, two assumptions are made. Firstly, it is assumed that the beats do not vary during the course of the acquisition session. Secondly, it is assumed that the waveforms can be correctly aligned in time. This alignment is generally carried out by identifying a fiducial point of the ECG beat. However, if the beats lack a fixed temporal relationship with respect to the fiducial point, then the averaged waveform will be smoothed and any high frequency details will be lost [8].

After the averaging step, the resultant signal is usually high-pass filtered to emphasize cell depolarization (which contributes the relatively high frequency components of the late potentials) and minimize the plateau and repolarization phases (which contribute the relatively low frequency components). Most studies employ a corner frequency of 40 Hz, as this setting has been shown to have a high predictive value [9]. In order to avoid filter artifacts, bidirectional filters are usually employed [10]. It should also be noted that a frequency domain based analysis technique has been developed [11]. Unlike its time domain counterpart, this technique can be employed in patients with intraventricular conduction delay of bundle branch block [12]. While both methods of analysis have been reported to facilitate patient risk stratification, the majority of the confirming studies have been carried out in the time domain.

While prospective studies have shown that the ability of SA-ECG to predict sustained ventricular arrhythmia is somewhat better than that of other methods (e.g. depressed left ventricular function), the positive predictive value of a positive SA-ECG is low (20-30%) [13]. Conversely, negative predictive values are on the order of 96-99% [13], illustrating the ability of SA-ECG identifying individuals who will not suffer adverse events.

2.   Methods

SA-ECG recordings were collected at rest using a customized SEER-MC card GE Medical Systems) that digitized the signals at 1,000 Hz with 12 bit A/D

resolution. The signals were acquired using orthogonal lead positions (Figure 2), which optimize the capture of the signal of interest regardless of its vectorial orientation [13]. In addition, this configuration also avoids the cardiac impulse that would introduce a repetitive motion artifact that would not be eliminated by the averaging procedure [10, 14].

At the completion of the acquisition session, the Holter data was downloaded to a PC workstation and analyzed using custom software developed in Matlab (The Mathworks Inc, Natick, MA). All subjects were at least 4 weeks post-MI, had left ventricular dysfunction, and were in sinus rhythm.
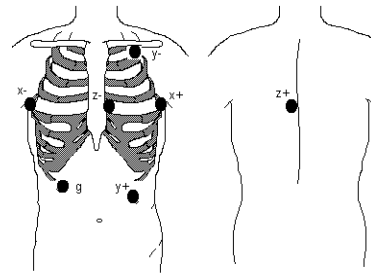

Figure 2: XYZ lead configuration employed for acquisition of the ECG data *(modified from: Wojcik ND[15]).*

The SA-ECG analysis was carried out according to the method developed by Simson [10]. Specifically, analysis began with the identification and alignment of the QRS complexes. A template matching technique was then employed to eliminate noisy and ectopic beats. The accepted QRS complexes were then used to calculate the averaged responses for each lead. The Z lead was used as the reference lead for all processing.

A target noise level of 0.5 was used as the end point in terms of determining the number of QRS complexes that were used to calculate the final vector magnitude signal. In addition, a fixed number of complexes (150) were also averaged, to keep in line with previous investigations [10].

After the averaging step, the QRS complexes were high-pass filtered to eliminate the low frequency components of the QRS complex. The filter corner frequency was set to 40 Hz. The QRS complexes were also low-pass filtered using a corner frequency of 250 Hz. Bidirectional filters were employed in order to avoid filter artifact. The averaged and filtered X Y and Z signals were then combined to yield a vector magnitude signal. The duration of the vector magnitude signal was then determined by identifying the start and end points of this signal. Each point was determined by searching for a 5

msec segment where the average signal amplitude exceeded the background noise by the mean noise level plus three standard deviations of the noise; the midpoint of the 5 msec segment was then used as the start or end point.

The sequence of steps from averaging to calculation of the duration was repeated using 100 different permutations of signals to from the averaged signal from which the calculation was derived. The mean and standard deviation of these 100 SA-ECG durations were then used as the summary statistic.

The signal analysis scheme is summarized in Figure 3, with an example of the typical output generated by the program shown in Figure 4.
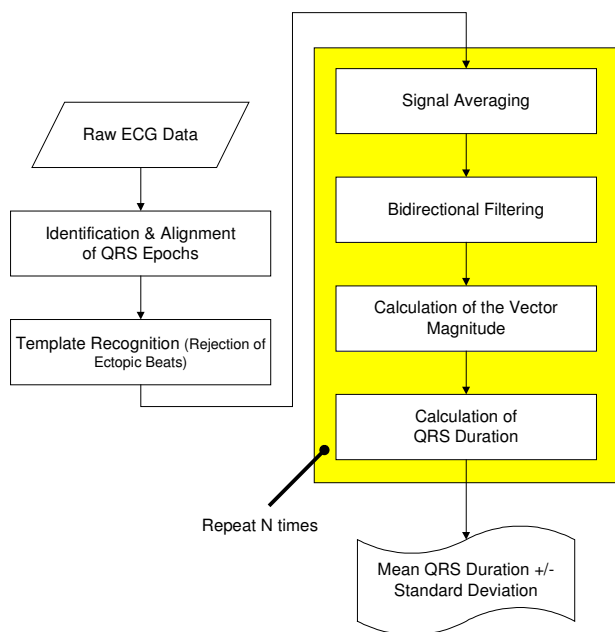

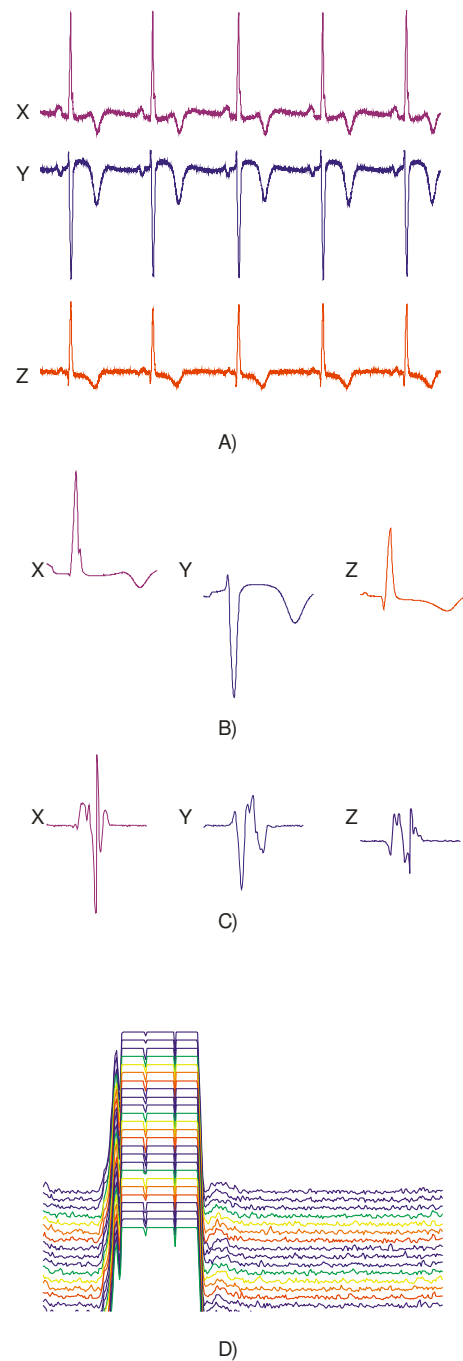Figure 3: Flowchart summarizing the SA-ECG analysis of the ECG data.

Figure 4: Figure illustrating the analysis steps. A) A 5 second sample of the X, Y and Z channels. B) Averaged X, Y and Z channels. C) Filtered versions of the averaged X, Y and Z channels. D) Sample XYZ vector signals calculated by using different permutations of signals from which the QRS duration summary statistics are calculated.

3. Results

Table 1 summarizes the results obtained using our analysis scheme in comparison to the standard analysis method in which only a single XYZ vector signal is used to calculate the QRS duration, LAS40 and RMS40.

In contrast to the standard analysis method which yields two possible classifications, our analysis adds a third "indeterminate" class which refers to a confidence interval that crosses the threshold levels established for QRS duration, LAS40 or RMS40.

Table 1: Summary of Results

	Standard SA-ECG	
	%Normal	%Positive
300 Templates 0.5 μV	50.00	50.00
noise level	52.56	47.44

Table 1 continued

	Modified SA-ECG		
	%Normal	%Positive	%Indeterminate
300 Templates 0.5 μV	35.90	43.59	20.51
noise level	43.59	37.18	19.23

4. Discussion and conclusions

As can be seen, a significant percentage of patients were classified as "indeterminate". This may partially explain the relatively low positive predictive value of SA-ECG. In particular, some patients initially identified as having prolonged QRS durations actually have ranges of QRS durations that at least partially fall within the normal limit.

The prognostic value of this method of SA-ECG analysis is being tested in a prospective multi-center study termed REFINE - Risk Estimation Following Infarction Noninvasive Evaluation.

Acknowledgements

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