Original Article

Ischemia detection by electrocardiogram in wavelet domain using entropy measure

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Abstract

BACKGROUND: Ischemic heart disease is one of the common fatal diseases in advanced countries. Because signal perturbation in healthy people is less than signal perturbation in patients, entropy measure can be used as an appropriate feature for ischemia detection.

METHODS: Four entropy-based methods comprising of using electrocardiogram (ECG) signal directly, wavelet sub-bands of ECG signals, extracted ST segments and reconstructed signal from time-frequency feature of ST segments in wavelet domain were investigated to distinguish between ECG signal of healthy individuals and patients. We used exercise treadmill test as a gold standard, with a sample of 40 patients who had ischemic signs based on initial diagnosis of medical practitioner.

RESULTS: The suggested technique in wavelet domain resulted in the highest discrepancy between healthy individuals and patients in comparison to other methods. Specificity and sensitivity of this method were 95% and 94% respectively.

CONCLUSIONS: The method based on wavelet sub-bands outperformed the others.

KEYWORDS: Ischemia, Electrocardiogram, Exercise Test.

Ischemia means lack of oxygen due to insufficient blood circulation. Ischemic heart disease is a condition with different causes which have one thing in common, the imbalance between the supply and demand of oxygen. This disease is one of the common fatal diseases in advanced countries.[1] Arteriosclerosis, which is a general phrase for thickening and hardening of artery wall, is one of the main reasons of mortality in most countries.[1] For epicardial coronary artery, it is the common cause of myocardial ischemia.[2] More precisely, in more than 90% of cases, ischemia is due to atherosclerosis.[3] Atherosclerosis is one type of arteriosclerosis that is developed in larger arteries and causes most cases of coronary artery disease, aortic aneurysm and arterial diseases of inferior limbs and it has an important role in cerebrovascular disease.[4-5] In addition, ischemia leads to certain changes of electrocardiography (ECG) signal such as electrical instability that may lead to ventricular tachycardia/fibrillation, and repolarization abnormalities identified by reversing T wave and displacing ST segment.[6-8]

Analysis of ECG signal has some problems such as lack of accurate and detailed information about cardiac electrical activity in all its

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levels and also lack of timely representation of information in critical and fatal diseases such as ischemia. However, it is widely used due to some advantages such as low cost and availability in all medical centers.[9] There are different methods for automatic finding of ischemic states using ECG signal including wavelet-based methods and time-frequency analysis,[10-16] techniques that are based on neural networks[17-19] and fuzzy systems,[20] methods using principal component analysis[21] and HMM-based techniques (hidden Markov model).[22] Although these methods have some advantages, they also have disadvantages such as the long time required and complexity in neural network learning or high sensitivity to noise and not timely diagnosis in some time-frequency analysis methods.

In this study, the existence of ischemia is investigated using entropy measure.[23] For this reason, 4 techniques in spatial and wavelet domains were considered to determine the optimal method having highest discrepancy between healthy subjects and patients. These methods were entropy analysis of ECG signal, entropy analysis of ECG signal in wavelet domain, entropy analysis of ST segments extracted from ECG signal, and entropy analysis of reconstructed signal using time-frequency features of ST segment in wavelet domain. The main contribution of this paper is finding a measure based on spatio-temporal analysis of ECG to determine the irregularity of ST segments. In the previous works, only some criteria such as entropy in signal domain were measured while in this study, after automatically extraction of ST segments, we tried to benefit from the advantage of spatio-temporal analysis of ECG signal to be able to calculate the irregularity of ST segments more precisely.

Methods

In this study a sample of 40 patients with mean-age of 55 ± 3 years (24 men) who had ischemic signs based on initial diagnosis of a medical practitioner (such as chest pain[24]) were selected. Finally, a the cardiologist evaluated and confirmed the results. We recorded ECG signals of patients at rest using 12-lead Cardiax[25] with sampling frequency of 500 (Figure 1) and ST deviation of 0.5 mm or variations of T-wave proposed as ischemic signs. For each signal, 10 beats were analyzed using entropy measures in order to predict who would be stress-test positive without having to undergo an exercise treadmill test (as the gold standard). To be able to evaluate these methods, exercise treadmill test was performed for all subjects that resulted in 22 cases (out of 40) with positive stress-test.

Since the entropy measure is a criterion to measure the irregularity, it can be used as a feature for distinguishing between ischemic patients (people with positive stress test) and healthy (people with negative stress test) without having to undergo a stress test. Figure 2 shows a sample ECG signal (one lead) of a patient and a healthy person. Entropy is one of the main measures used in information theory.[26] It is used for measuring uncertainty in random variables. The highest uncertainty indicates the highest amount of information. The entropy of a discrete variable X with probability density function $P_x(x)$ is defined as follows:

$$H(x) = -\sum_{x \in X} P_x(x) \, Log P_x(x) \quad (1)$$

H(x) is maximized when all occurrence of an experiment have the same probability (uniform distribution) and is zero when probability of one occurrence is explicitly one (delta distribution).

Since ischemic signals have more perturbations and are more chaotic in comparison to non-ischemic signals, entropy can be used as a measure for classifying ischemic and non-ischemic patients. The entropy has been usefully applied, for example, in analyzing variation in R-R interval sequences.[27-34] However, we do not know whether it can also be applied to morphologic variation across a set of ST segments extracted from sequential beats. To justify the connection between the concept of entropy as a measure of uncertainty used in information theory and its use as a measure for classifying ischemic and non-ischemic patients we used goodness of fit test.[35] While the good-

Patient protection:	floating common (IEC-601, BF type)
Defibrillator protection:	5 kV (max. 1 kV/msec)
Resolution:	2.44 uV/bit (12 bit A/D)
Input impedance:	10 MOhm
CMRR:	120 dB
Filters:	150 Hz low pass (hardware, constant)
	50, 100 Hz (software, switchable)
	60, 120 Hz (software, switchable)
	35 Hz (software tremorfilter, switchable)
Time constant:	1.6 sec
Linearity error:	<0,5%, < 1/2 LSB
Polarization voltage:	400 mV
Leads:	12 Standard + 3 Frank
Power consumption:	+ 5 V : 210 mA, +12 V : 70 mA

Figure 1. Specifications of Recorded ECG

ness of fit value for patients was 541.57 ± 36.28, it was 882 ± 41.54 for healthy subjects illustrates the difference between uniform distribution and histogram of ECG signals of patients and healthy persons using chi-square test.[36] It shows that there was a significantly different degree of random variability in ischemic populations as opposed to non-ischemic ones, and that the probability distribution was more uniform in one group than the other.

In this study four states were proposed for calculation of the entropy in order to obtain the state with highest discrepancy in entropy of healthy and patient subjects. These four states included:

1) Entropy analysis of ECG signal

In the first part, merely analyzing ECG signal of subjects in time domain is proposed. For this reason, entropy measure of all data is calculated. General structure of this part is as follows:

1- Entropy measures for each lead of ECG signal are measured individually. For each signal 10 beats are analyzed using the first (1) equation.

2- The average of obtained values in previous step for 12 leads is considered as total entropy of each person.

3- The obtained value in previous step is compared to a threshold. If it is more/less than the threshold we consider this case as patient/healthy person.

2) Entropy analysis of ECG signal in wavelet domain

The principle of discrete wavelet transformation (DWT) is related to sub-band coding originally introduced in 1976.[37] To apply DWT, at first the signal is passed through a half band low pass digital filter with pulse response h[n]. Therefore, the frequency components higher than half of the highest frequency of signal are removed due to this filtering. Since the highest frequency in filter output is π/2, thus the length of signal would be halved by removing samples alternatively without losing any information. A similar procedure is performed with a half band high pass digital filter g[n]. Hence, in first step output of DWT are two "low pass" and "high pass" signals with decreased length (half) of original signal as follows:

$$Y_{high}[k] = \sum_n x[n]g[2k-n] \quad (2)$$
$$Y_{low}[k] = \sum_n x[n]h[2k-n] \quad (3)$$

Consequently, in this stage a time resolution is halved while frequency resolution is doubled. This procedure can be applied again on low pass sub-band and in each step,
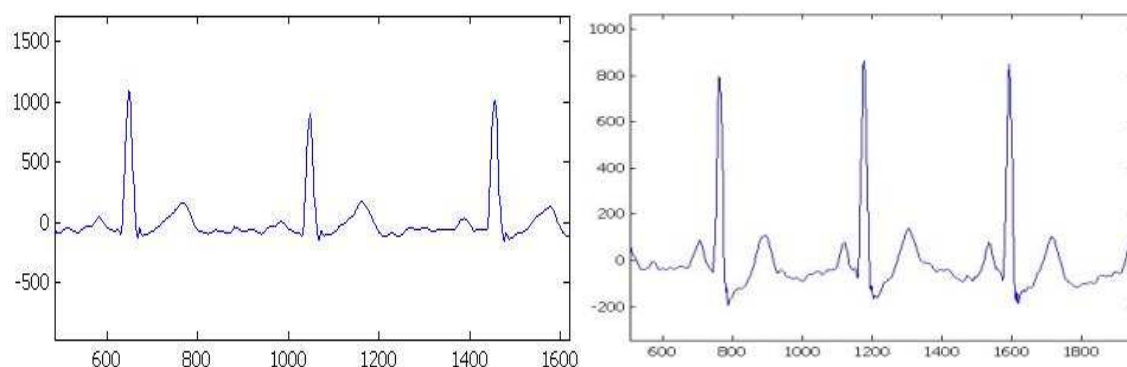
Figure 2. A Sample ECG signal of a patient (Left) and
a sample ECG signal of a healthy person (Right)

frequency resolution is doubled by halving time resolution. Generally, increasing level of entropy is due to the increasing perturbation in respective area, and this increases the probability of ischemia existence in respective area.

In this part, to obtain the entropy measure, the ECG signals are transformed to DWT domain and other operations are performed on produced signals from appropriate sub-bands in this domain. The main reason of using DWT is its power for separation of various time-frequency components in its sub-bands. Accordingly, DWT is an appropriate tool for distinguishing between unnecessary components (such as noise) from signal. After applying DWT on signal (performed in 4 levels and using Daubechies wavelet 4[37]), it is required to use one of the produced signals from appropriate sub-bands as a reference in order to perform other processing operations on this signal.[13] In this paper, according to figure 3, the reconstructed signal merely using sub-bands of last stage is named "Approximate 1". "Approximate 2" is obtained by incorporating details of sub-band of previous stage for reconstruction, and consequently "Approximate 3" and "Approximate 4" are acquired using details of sub-bands of previous stages. The entropy is evaluated for these produced signals. The signal with higher entropy in patient subjects (indicating more perturbation) and the signal with lower entropy in healthy subjects (indicating less perturbation) are selected based on this fact that signal perturbation in

healthy people is less than signal perturbation in patients.

The main steps of proposed method in this section can be described as follows:
1- To apply DWT to ECG signal for each lead
2- To calculate the entropy of "Approximate 2" for each lead.
3- To average out the obtained entropy measures from leads.

The signal with average entropy higher than a threshold is defined as ischemic case based on this fact that signal perturbation in healthy people is less than signal perturbation in patients.

3) Entropy analysis of ST segments extracted from ECG signal

In this section, entropy measurement is performed with respect to ST segments extracted from ECG signals of patients and healthy subjects in order to achieve more accurate analysis of entropy. For this reason, ST segments are extracted for each lead (for each signal 10 beats are proposed) and their entropy measures are averaged (over all segments) to obtain the mean entropy for each case.

The first step in ST segment extraction is extraction of R wave. In this study adaptive threshold limit algorithm[38] was used for R peak detection. It is designed using a pair of threshold limits called "up limited threshold (ULT)" (Eq. 4) and "down limited threshold (DLT)" (Eq. 5). If the numbers of peaks detected by ULT and DLT in each threshold step are not equal, error component is calculated
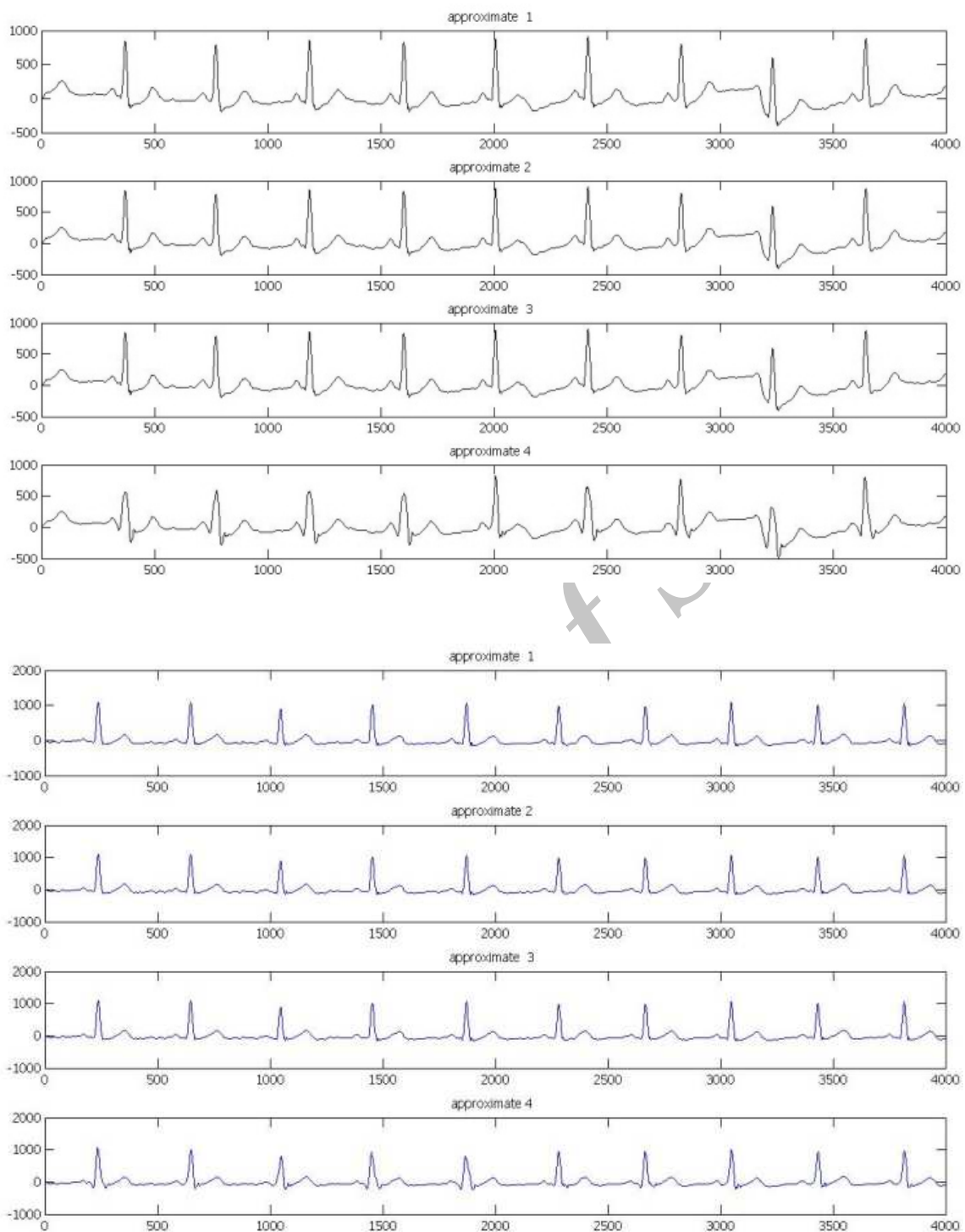
Figure 3. First four rows shows the approximate sub-bands of a patient and the next four rows illustrates the approximate sub-bands of a healthy person

and subtracted from limits and new thresholds are obtained. This repetition continues until these two limits equal and at last final threshold limit is specified.

$$TH_{m+1} = TH_m - W_m\Delta \quad (4)$$

$$TH_{f+1} = TH_f - W_f\Delta \quad (5)$$

In above equations TH_{m+1} and TH_{f+1} are modified threshold limit values, TH_m and TH_f are initial threshold limit values, and $\Delta = |TH_f - TH_m|$ is the difference between two determined limits. W_f and W_m are error weight factor which in each step have specific value

with respect to number of false detected peaks. J point detection is done after specifying R point in desired signals. Thus, after detection of these two points (points related to R wave and J point) extraction of ST segment can be performed.[9] In this respect, after extraction of J point, 80 and 120 milliseconds after that is considered (respectively for healthy people and tachycardia patients) as the end of component (or start of T wave).[39] Figure 4 shows a comparison between the ST segments of a patient and healthy people.

According to our explanation in this section, the proposed method is a refinement of the first method and analyzes just the ST segment of the time-domain waveform rather than the entire beat. The main steps of proposed method can be described as follows:
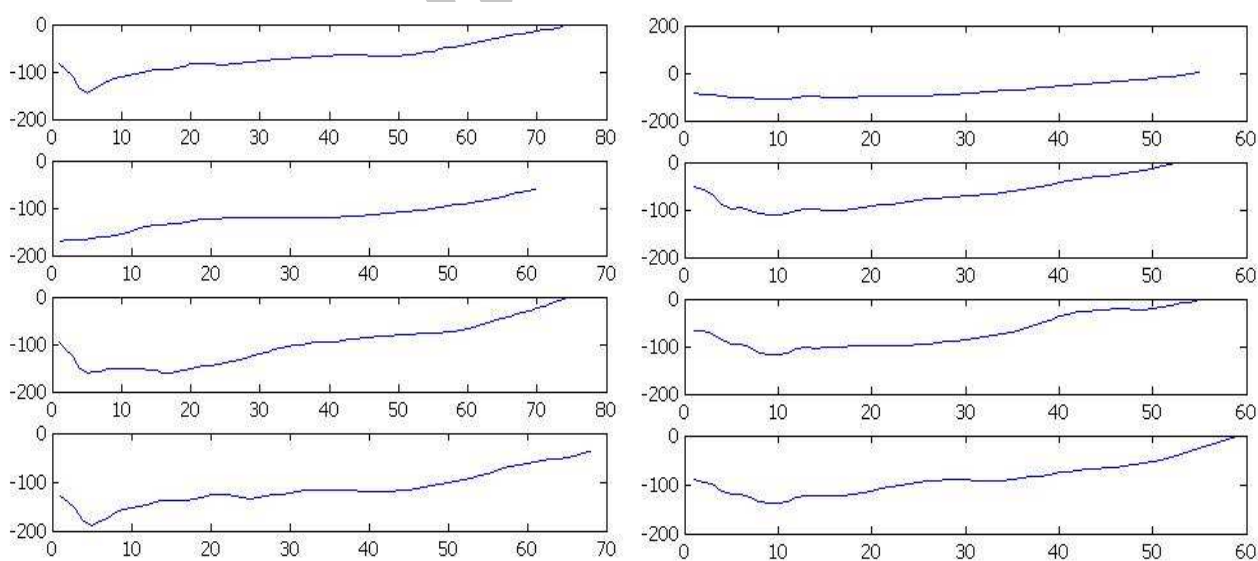
1- Extract the ST segment of 10 beats of ECG signal of each lead.

2- Measure the entropy of extracted signal in previous step using (1).

3- Calculate the average of obtained values in previous step for all 12 leads in order to obtain the total entropy of each person.

4- The obtained value in previous step is compared to a threshold. If it is more/less than the threshold we consider this case as patient/healthy person.

4) *Entropy analysis of reconstructed signal from time frequency features of ST segment in DWT domain*

In this section, in order to more accurate analysis of ECG signal, after transforming signal to wavelet domain, since ST segment frequency is about 30-40 Hz, second sub-band including 30-60 Hz frequencies is selected as reference sub-band.[13] Then ECG signal is reconstructed using only filtered version of this sub-band. After signal reconstruction, entropy measure related to this signal is measured and a comparison is done between data of healthy and patient subjects. The proposed method in this section is a refinement of the second method and uses a wavelet-filtered version of the original waveforms to accentuate the ST feature. The main steps of proposed method can be described as follows:

1- To apply DWT to ECG signal for each lead

2- To reconstruct the signal using (only) filtered version of the second sub-band

3- To calculate the entropy of reconstructed signal in previous step for each lead

4- To average out the obtained entropy measures from leads

Figure 4. Extracted ST segments of 4 beats of ECG signal in a patient (Left column) and a healthy person (Right column)

The signal with average entropy higher than a threshold is selected as ischemic case based on this fact that signal perturbation in healthy people is less than signal perturbation in patients. Figure 5 illustrates a sample of reconstructed signal for a patient and a healthy person. Note that we can produce more appropriate signals according to time-frequency properties of ST segment using wavelet packet.

Results

We used a gold standard of the exercise treadmill test, with a sample of 22 patients who were stress-test positive and 18 who were normal. The goal was to predict who would be positive without having to under-go a stress test. Table 1 shows entropy measures obtained using proposed methods in this paper for both patients and healthy people. As it can be observed from the obtained results in table 1, discrepancy between obtained components from ECG signals was less than results obtained from extracted sub-bands. In addition, in ST segments extracted from signals and reconstructed signal from time-frequency properties of ST segments in wavelet domain, the average entropy obtained from healthy subjects was less than patients. Considering different states among all patients of the study, it was observed that discrepancy between components obtained with respect to first (ECG signal analysis), third (ST segments analysis) and fourth (analysis of reconstructed signal from time frequency features of ST segment in DWT domain) methods was less than results obtained from sub-bands of wavelet (second method). For methods 1 to 4, the correlation with stress test was 75, 95, 67.5 and 50, respectively. These correlation coefficients confirm this outcome by comparing the correlations between results of stress test and pro-posed methods in this paper for ischemia detection.

According to these findings, it can be observed that entropy measurement for above groups suggests that since perturba-tion in patient's signals with positive stress test was more than subjects with negative stress test (due to existence of irregular ST segments and/or QRS complexes), obtained entropy measures had higher levels. As it can be seen in table 1, the highest discrepan-cy occurred in second method (entropy anal-ysis of ECG signal in wavelet domain) and thus this method is the optimal one for ischemia diagnosis. Table 2 shows the sensi-tivity and specificity of all methods used in this paper. Comparing the results of this ta-ble with table 3 which shows the results of other methods introduced in other studies,[23, 40-43] we can conclude that our methods out-performed previous techniques.

Discussion

In this paper the entropy measure is pro-posed as a feature for ischemia detection in order to estimate significant ST-segment dev-iation in exercise test. For this reason, entro-py was measured using four manners, i.e. using ECG signal directly, using wavelet sub-bands of ECG signals, using extracted ST segments, and using reconstructed signal from time-frequency feature of ST segments in wavelet domain. Our simulations showed that proposed method based on wavelet sub-bands outperformed the others.

In this study we only used Daubechies wavelets. Using other transforms such as undecimated wavelet and complex wavelet[44] (that have shift invariant property) or wave-let packet (that is able to better specify time-frequency properties of ST segments) could improve the results. In addition, a similar entropy-based manner can be used for detec-tion of other heart diseases such as myocar-dial infarction (MI). Moreover, we used stress-test as a gold standard. It is clear that stress-test may result in incorrect results and better evaluation could be achieved using angiography as a gold standard.

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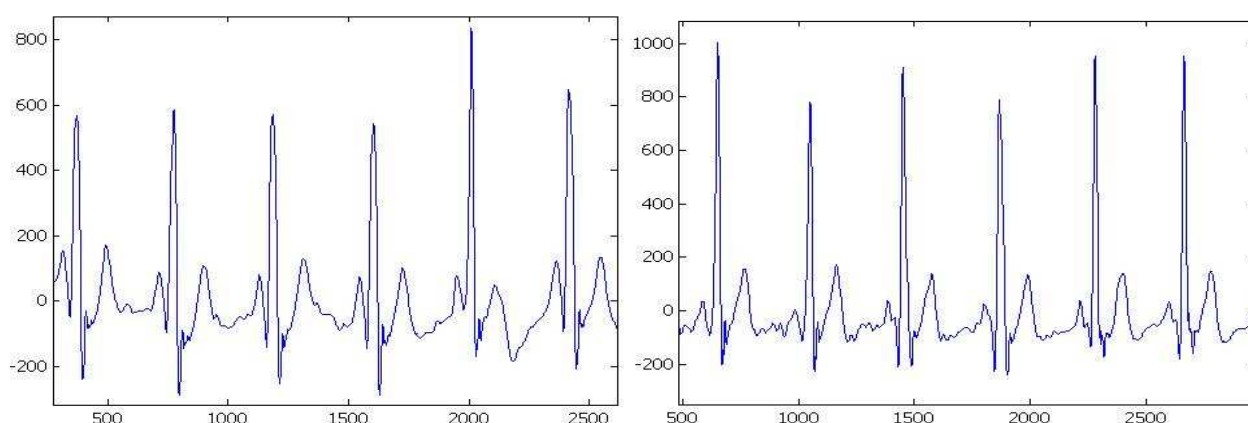
Figure 5. Reconstructed signal from time frequency features of ST segment in DWT domain of a patient and healthy person in a patient (Left), and a healthy person (Right)

Table 1. Comparison between Entropy of Proposed Methods for all participants in This Study

Method		Patient	Healthy
Entropy Analysis of ECG Signal		8.186 ± 0.010	7.710 ± 0.011
Entropy Analysis of ECG Signal in Wavelet Domain	Approximate 1	8.583 ± 0.015	7.674 ± 0.018
	Approximate 2	8.601 ± 0.019	7.596 ± 0.021
	Approximate 3	8.435 ± 0.014	7.579 ± 0.017
	Approximate 4	8.399 ± 0.021	7.911 ± 0.030
Entropy Analysis of ST Segments Extracted from ECG Signal		4.591 ± 0.016	4.253 ± 0.020
Entropy Analysis of Reconstructed Signal from Time Frequency Features of ST Segment in DWT Domain		8.963 ± 0.013	8.799 ± 0.016

Table 2. Comparison between Sensitivity and Specificity of proposed methods

Method	Sensitivity	Specificity
Method 1	81	66
Method 2	95	94
Method 3	68	66
Method 4	54	44

Table 3. Sensitivity and Specificity of the Methods used by other studies

Method	Sensitivity	Specificity
Taddei [32]	84	81
Vila [33]	83	75
Jagger [34]	87	88
Maglaveras [35]	89	78
Andreao [15]	83	85

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

EF and AF participated in most of the experiments and carried out all the experiments. HR carried out the design and coordinated the study and prepared the manuscript. AMD provide assistance in the design of the study and participated in manuscript preparation. MPM provided assistance for all experiments. All authors read and approved the content of the manuscript.

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