QRS Fragmentation Index as a New Discriminator for Early Diagnosis of Heart Diseases

Francisco-Manuel Melgarejo-Meseguer [1], Mariela Salar-Alcaraz[1], Zaida Molins-Bordallo[1], Francisco-Javier Gimeno-Blanes[2], Estrella Everss-Villalba[1], José-Antonio Flores-Yepes[3], José Luis Rojo-Álvarez[4,5], Arcadi García-Alberola[1]

[1] Hospital Clínico Universitario Virgen de la Arrixaca. Unidad de Arritmias, Murcia, Spain
[2] Departamento de Comunicaciones. Universidad Miguel Hernández, Elche, Spain
[3] Escuela Politécnica Superior de Orihuela. Universidad Miguel Hernández, Elche, Spain
[4] Center for Computational Simulation, Universidad Politécnica de Madrid, Spain
[5] Departamento de Teoría de la Señal y Comunicaciones. Universidad Rey Juan Carlos, Spain

Abstract

In the past few years, the presence of fragmentation in the QRS complex has been demonstrated to be related to diseases such as myocardial fibrosis, cardiac sarcoidosis, arrythmogenic cardiopathies, acute coronary syndrome, and Brugada syndrome, among others. The detection of fragmentation in the QRS is usually carried out manually, which represents a subjective pattern recognition task that demands an effort by the clinician, increasing with the number of patients. These problems have made the process of fragmentation detection a good candidate to its automatization. In this work, we used a database with over six-thousand 12-lead ECG from Hospital Virgen de la Arrixaca de Murcia (Spain), which where digitally recorded with GE MAC5000. Affected and non-affected patients records were extracted for computerized analysis. Clinical supervision was performed for gold-standard development and for signal classification. Fragmentation detection algorithms were developed using first and second derivatives calculation in the pre-qualified segments of the signal, after fiducial point detection. The obtained results were 96.88% sensitivity , 72.92% specificity, and 82.50% accuracy. These results confirm that it is possible to automatically detect fragmentation, constituting a relevant tool to pre-qualify patients for further diagnostic-tests, and it also opens new opportunities for computerized diagnosis.

1. Introduction

The most common myocardial disorder is the Hypertrophic Cardiomyopathy (HCM), which is characterized by the increase of the heart wall thickness (hypertrophy), when it is not being due to extra muscular causes such a hypertension or valvulopathies. HCM is considered a hereditary disease and its affects to 50% of descendants. This disorder can not always be detected because it is often asymptomatic, and when it is not, the most common symptoms are extensively replicated in a large number of other illnesses. Its symptoms are fatigue, palpitations, chest pain, and faints. From a physiological viewpoint, one of the characteristic of HCM is the myocardial fibrosis. Recent research has proven also that HCM is correlated with the risk to develop ventricular arrhythmias, heart failure, and sudden cardiac death [1–5].

HCM diagnosis can be performed with a physical exploration, and the disorder appears as a heart murmur in 50% of patients. Another way to detect HCM is by careful visual inspection of the ECG, as fragmentation in the QRS complexes is often present. Fragmentation is understood and defined as the existence of small peaks or notches in the QRS complex regions, as it is shown in Figure 1.

Detection of HCM by an expert clinician is an effort intensive task, as it requires careful clinician willing to seek for this kind of events in the electrical signal over all leads, as it can be easily confused with simple impulse noise. This time consuming effort cannot always be devoted, as

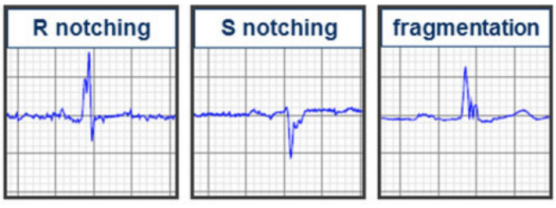

Figure 1: Examples of the most commons types of fragmentation that can present in the ECG.

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clinicians frequently work with large groups of patients. Therefore, an automated process to reduce negative detections and to limit the number of cases to be reviewed is required by clinicians.

Therefore, the aim of this work is to design and implement an algorithm that allows us to detect the fragmentation in the QRS complexes in order to make efficient the expert time for diagnosis of HCM in large populations. For the development of this algorithm, we worked together with medical doctors (MDs) from Hospital Universitario Virgen de la Arrixaca (HUVA) of Murcia, who closely supported and supervised the creation of a gold-standard and the evaluation of the proposed fragmentation detection algorithm. For that purpose, we developed a fragmentation detector taking into account pre-detected fiducial points, the evaluation of signal derivative, and the medical knowledge about this disorder. In order to evaluate this algorithm, we used an ECG database, collected and carefully annotated by MDs from HUVA. In order to score the developed algorithms, several merit figures were used for comparison and statistical benchmark namely, sensitivity, specificity, and accuracy.

This paper is structured as follows. In the Section 2, we describe and explain the used database , the recording devices, and the different steps of our algorithm. Then, in Section 3, we develop and illustrate the experiments and results. Finally, Section 4 includes the discussion and conclusions of this work.

2. Materials and methods

2.1. Equipment and algorithm overview

The set of records used in this work were selected from a database of six-thousand records, and they were carefully annotated by expert clinicians from HUVA. This set was carefully selected by clinicians including already diagnosed subjects from HCM and control cases. The subset includes a total of 80 records, where 40 records showed pre-annotated fragmentation and 40 were control records. All registers were acquired using the *GE MAC 5000* from General Electric, which stores the 12-leads at 500 Hz sampling rate.

The implemented algorithm can be split into in three key blocks, namely, **pre-processing**, **intra-lead detection**, and **fragmentation detection**.

The **pre-processing** stage has three additional parts. The first one is the *detection of QRS complexes*, where a 50 Hz cut-off low-pass filter is applied to the signal. We used a very low order to preserve the fragmentation wave forms in the ECG. Then, the low-pass filtered signal is processed for baseline noise removal. After this, a characteristic signal is computed, which contains enhanced QRS complexes and where the R-waves can be easily thresholded. Finally, the detection of QRS complexes is performed by using the characteristic signal, the threshold, and the medical knowledge about the heart behavior and for this purpose we used previous published work from our team [6].

The second part of the **pre-processing** stage is the *computation of the ECG pattern*. Physiologically, the existence of fragmentation in the ECG is mainly due to scars in the myocardial tissue, and for this reason, the fragmentation must be seen replicated along the complexes of a given lead and also along several leads, at least in those corresponding to the same side-projections of the cardiac electrical signal. For that reason, we implemented a process that creates a beat template by taking into account all the complexes in every lead. The *computation of the ECG pattern* begins with the selection of the QRS complexes keeping the synchrony in the RR, and also excluding all those ones previous and next to the ectopic beats. The next step is the selection of the QRS-wave region. We selected a region around the QRS complex in beats meeting the previously described conditions, corresponding to the 33% of the heart rate value before the R-wave, and the 66% of the heart rate value after it. Then, a subregion inside each QRS complex is selected in order to compare the waveform in terms of the correlation coefficient. We choose 10% duration around the R-peak for this purpose and only beats corresponding with a correlation over 0.995 were considered as valid, as they did not include large noise. Finally, valid beats were averaged in order to create the denoised ECG template. This ECG pattern contains all the relevant information, with a very low amount of noise, as it was described in [7]. An example of this computed ECG pattern can be seen in Figure 2.

The last part of the **pre-processing** stage is the *detection of the fiducial points*, namely, QRS onset, peak of Q wave, peak of R wave, peak of S wave, peak of R' wave, and QRS offset. In this stage, we used the previously described pre-computed ECG template. Then, we evaluated the signal activity according to [7], creating a curve, to pre-qualify the candidate region of QRS waveform. After that, the QRS onset and offset were chosen by using the empirical threshold over the curve computed in the previous step. Then, the QRS onset and offset were fine-tuned by using the minimum angles before and after the fiducial points pre-selected by thresholding, and if these angles were classified as to small, the points were not considered as onset/offset, which allowed us to avoid mistakes in the detection due to small notches. After onset and offset detection, all the other wave peaks were evaluated by using of the first and second derivate in order to find the local maxima and minima in the region between the onset and offset. First local maximum was set as R wave according to clinical definition, as well as S was set as the first minimum after R, Q point was set as the lowest minimum

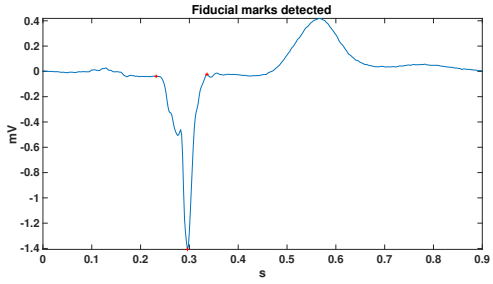

Figure 2: Detected fiducials marks on the ECG pattern.

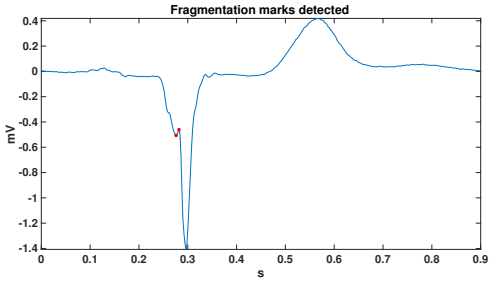

Figure 3: Detected F-points on the ECG pattern.

before R and after OnSet, and R point was set as the highest maximum between the S point and the QRS offset. All other local maxima and minima were not considered at this point, and will be evaluated in future analysis. An example of the detection of fiducials marks is shown in Figure 2.

The next stage is known as **intra-lead detection**, and it can be divided in three different parts. The first one is the *ECG pattern pre-process*, in which the ECG template is differentiated and normalized to ± 1. A new variable, which contains a version of the ECG template that is high-pass filtered with a cut-off frequency of 40 Hz, is next created. This new variable is to be used later as a noise level index in order to set the level of fragmentation that could be evaluated. The second part of this stage is known as *extreme points detection*, and the normalized-derivative of the ECG pattern is sectionalized according to the previously computed fiducial points. For each segment, the local minimum and maximum are again detected using a zero-crossing detector, and we will refer to this points as *extreme-point*. The next part of this stage is the *extreme-point tuning*, where the amplitude value of every single extreme point are compared against the weighted root mean square value of a portion of the ST segment in the high-pass filtered ECG pattern computed before, which will be called here *noise index*. So, for the purpose of this work, all extreme points not reaching a certain threshold against the noise index, were not considered as valid information for the fragmentation analysis. Finally, after removing the non-valid extreme points, the remaining points are considered as fragmentation points or *F-Points*, as its shown in Figure 3.

As we mentioned before, the fragmentation has to do with physiological reality in the heart tissue, and due to this fact, a last processing stage, is required for final fragmentation classification which compares the results of F-points among regions of the leads. For that purpose, in this stage we combine all the leads corresponding to side-projections of the heart electrical activity and they are evaluated as separate regions, namely: (i) I, aVL, V5, and V6 are considered as lateral leads; (ii) II, III, and, aVF are inferior leads; and (iii) V1, V2, V3,V4 are anterior-septal leads. For each region, we considered the existence of fragmentation when F-points are detected at least in two leads.

3. Experiments and results

Before starting with the experiments and results section, we need to present the different values that are going to be used in order to score our detector. These values are:

- Sensitivity (S) is the rate of positives that are marked as such by our detector, and it is calculated as:

$$S = \frac{Tp}{Tp + Fn} \tag{1}$$

- Specificity (Sp) is the rate of negative that are marked as such by our detector, and it is calculated as:

$$Sp = \frac{Tn}{Tn + Fp} \tag{2}$$

- Accuracy (Ac) is the rate of successes detection (positives and negatives) that are marked as such by our detector, and it is calculated as:

$$Ac = \frac{Tp + Tn}{Tp + Fn + Tn + Fp} \tag{3}$$

where Tn is the number of real no fragmented ECG marked as no fragmented by our detector, Tp is the number of real fragmented ECG marked as fragmented by our detector, Fn is the number of real fragmented ECG marked as no fragmented by our detector, and Fp is the number of real no fragmented ECG marked as fragmented by our detector.

As we have seen in Section 2, the method presented in this work has an important coefficient that must be tunned in order to get good results,and this value is the weight coefficient ρ used to discard some detected F-points because of the noise present in the signal.

Figure 4 shows the behavior of the fragmentation detector for different values of ρ. The ρ value was set at 2.2 because our detector achieved 96.88% S, 72.92% Sp, and 82.50% Ac.

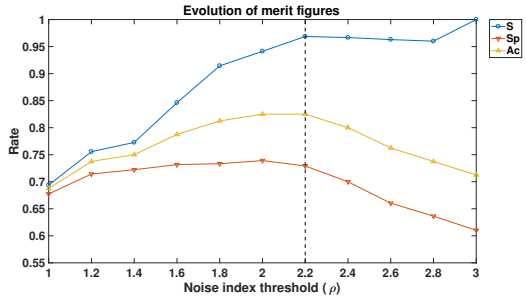

Figure 4: Evolution of S, Sp, and Ac for different values of ρ.

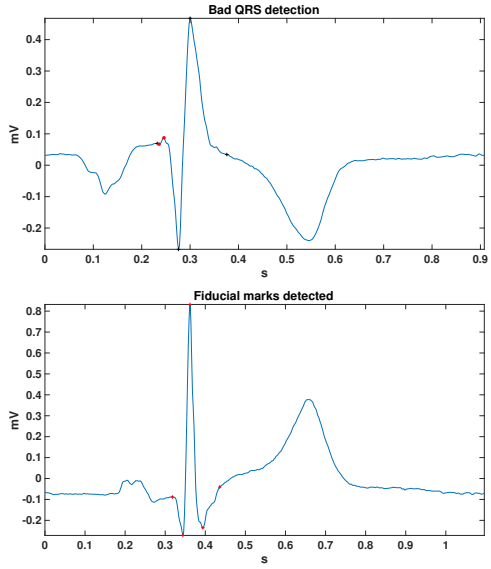

Figure 5: False positive due to failure in the detection of fiducial points (up), and false negative due to not detection of F-point in the right flank of S-wave for noise in ST segment.

Despite the good results shown by our algorithm, we know that the detector can be improved in order to avoid different kinds of errors that it currently has, and one of the most important errors in the fragmentation detection is due to a bad QRS onset/offset detection, as shown in Figure 5. Also the weighted root mean square value is useful to remove fakes F-points, but in some cases it is not sufficient, and it represents another source of errors.

4. Conclusion

As we saw in Section 3, the results of this detector are good enough to consider it as tool for automatic detection of fragmentation in medical practice.

In order to improve our detector, we consider that some future research lines in this setting are the use of advance techniques, as neural networks or support vector machines or deep learning, and the application of this detector in new types of records, such a Holters, long term monitoring, or wearables records.

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Address for correspondence:

Francisco-Javier Gimeno-Blanes
Innova Bld., Av. Univesidad, s/n,
03202 Elche Alicante, Spain
javier.gimeno@umh.es