Organization Analysis of Atrial Fibrillation Applied to the Improvement of Electrical Cardioversion Protocols

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Abstract

Predicting non-invasively the effectiveness of a shock in external electrical cardioversion (ECV) is clinically relevant to enhance these protocols in the treatment of atrial fibrillation (AF). The present contribution analyzes the ability of a non-linear regularity index, such as sample entropy (SampEn), to follow-up noninvasively AF organization under successive attempts of ECV and to predict the effectiveness of every single shock. Results showed that, after each unsuccessful shock, a SampEn relative decrease was observed for the patients who finally reverted to normal sinus rhythm (NSR), but the largest variation took place after the first attempt, thus indicating that this shock plays the most important role in the procedure. Indeed, by considering jointly the patients who needed only one shock and the patients who needed several shocks, 91.67% (22 out of 24) of ECVs resulting in NSR, 93.55% (29 out of 31) of ECVs relapsing to AF during the first month and 100% (10 out of 10) of ECVs in which NSR was not restored were correctly classified. As conclusion, AF organization analysis via SampEn from the surface ECG can provide useful information that could improve the effectiveness of conventional external ECV protocols used in AF treatment.

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, accounting for approximately one-third of hospitalizations for cardiac rhythm disturbances [1]. To revert AF back to normal sinus rhythm (NSR), electrical cardioversion (ECV) is the most effective alternative and consists of delivering a controlled transthoracic electrical shock to the patient [2]. The prediction of NSR maintenance before the ECV procedure is clinically very interesting because, approximately, 40–60% of the cardioverted patients revert back to AF within the three months subsequent to ECV and around 60–80% within one year [2]. Moreover, it would be notably interesting and advantageous to carry out this prediction from the analysis of non-invasive recordings, as surface ECGs, because they can be easily and cheaply obtained and could avoid the risks associated to invasive procedures. In this respect, a method to predict non-invasively the ECV outcome before it is attempted has been recently proposed with a diagnostic ability of 94% [3]. This technique quantified AF organization by using a non-linear regularity index, such as sample entropy (SampEn) [4]. However, the method has only been validated making use of a database composed by patients who underwent one ECV attempt. Since, in the selected cases, NSR was restored after the first shock, the method's ability to predict both the ECV result when several shocks are delivered and to evaluate the arrhythmia progressive organization, have not addressed yet.

Nonetheless, organization follow-up during successive attempts of ECV may lead to clinically useful information about AF cardioversion that, at this moment, is not considered by conventional external ECV protocols [2,5]. In fact, under these protocols, the effects of unsuccessful shocks are not taken into account for the application of consecutive attempts [2]. Although the costs and patient's suffering associated to the delivery of one or several shocks are minimal, the risks are increased [2, 6]. Overall, the present contribution focuses on analyzing the ability of SampEn to follow-up AF organization under successive attempts of ECV and predicting the effectiveness of every single shock.

2. Methods

2.1. Study population

Sixty-three patients (20 men and 43 women) with persistent AF lasting for more than 30 days, undergoing ECV were followed during four weeks. All the selected patients in the database were under antiarrithmic drug treatment with amiodarone (200 mg/day) before the procedure and during the whole follow up after ECV. Moreover,

Parameters	Only one shock		Several shocks		
	NSR maintenance	AF Recurrence	NSR maintenance	AF Recurrence	Unsuccessful ECV
Patients	14	21	8	10	10
Men	4 (28.57%)	8 (38.10%)	2 (25%)	4 (40%)	2 (20%)
Underlying heart disease	2 (14.29%)	5 (23.81%)	2 (25%)	2 (20%)	2 (20%)
Sustained AF duration (months)	9.5 (1–36)	10.5 (1–54)	9.7 (1–39)	9.9 (1–41)	10.7 (1–46)
Left atrial diameter (mm)	43.88 ± 8.26	46.23 ± 6.20	45.15 ± 5.02	42.28 ± 6.23	44.42 ± 4.39

Table 1. Clinical characteristics and measured parameters in the population under study.

all of them were also under anticoagulant treatment with acenocumarol (INR between 2.5 and 4). A standard 12–lead ECG was acquired during the entire ECV procedure. The signals were digitized at a sampling rate of 1024 Hz with 16–bit resolution.

In 35 patients (55.56%), only one electrical shock with an energy of 200 J was needed to revert AF back to NSR. After ECV, in 21 patients (60%) NSR duration was below one month, whereas in the remaining 14 (40%) NSR was maintained. On the other hand, between 2 and 4 shocks with an energy of 300, 360 and 360 J, respectively, were needed to revert AF in 18 patients (28.58%). In this case, 10 patients (55.56%) relapsed to AF, whereas the remaining 8 patients (44.44%) continued in NSR during the whole study follow up. In only 10 patients (15.87%), NSR was not restored after the 4 consecutive electrical shocks. The median arrhythmia duration was 10.58 months (range 1–47.22) and echocardiography demonstrated a mean left atrium diameter (LAD) of 45.82 ± 6.93 mm. Moreover, 20.63% of the patients presented underlying heart disease. A summary of these parameters is shown in Table 1.

2.2. AF organization estimation

Lead V_1 was chosen for the analysis because previous works have shown that atrial activity (AA) is prevalent in this lead [7]. The recordings were preprocessed in order to improve later analysis. Firstly, baseline wander was removed making use of forward/backward highpass filtering with 0.5 Hz cut-off frequency. Secondly, high frequency noise was reduced with an eight-order forward/backward IIR Chebyshev lowpass filtering, whose cut-off frequency was 70 Hz. Finally, powerline interference was removed through adaptive notch filtering, which preserves the ECG spectral information [8].

To estimate AF organization, the application of SampEn to the surface ECG requires the fulfillment of several steps. Firstly, the ventricular activity has to be removed making use of a cancellation technique [3]. Next, the main atrial wave (MAW) has to be extracted from the AA by applying a selective filtering centered on the dominant atrial frequency (DAF), i.e. the highest amplitude frequency within the 3–9 Hz range. Finally, SampEn computation can be applied to this wave with $m = 2$ and $r = 0.25$ of its standard deviation. This approach has been described in detail in previous works [3, 9]. Finally, AF organization was computed for a 10 seconds-length AA segment preceding every shock delivered to the patient selected.

2.3. Statistical analysis

Results are expressed as mean $\pm$ standard deviation for all the segments belonging to the same group and the t Student test was used to determine whether there was any significant difference between the groups. A two–tailed value of $p < 0.01$ was considered as statistically significant.

Thresholds to predict the shock effectiveness and AF recurrence were obtained making use of the patient set in which several shocks were applied. Precisely, the maximum discrimination thresholds between effective and ineffective ECVs (Th1) and between patients who relapsed to AF and resulted in NSR, after the first month (Th2), were obtained by computing the corresponding receiver operating characteristic (ROC) curve over the obtained SampEn values before the second shock, such as will be described in next section. For each case, different thresholds or cut-off points were selected and the sensitivity–specificity pair for each one of them were computed. The closest point to 100% sensitivity and specificity was selected as optimum discrimination threshold.

3. Results

Regarding the patients who needed several shocks to restore NSR, the AA organization values computed with SampEn are shown in Fig. 1. The MAW SampEn values obtained for the segments preceding each ECV attempt are presented. As can be appreciated before the first shock, all the patients presented overlapped SampEn values, thus making difficult their discrimination. On the contrary, a threshold (Th1 $= 0.1223$) can be established for discriminating between effective and ineffective ECVs before the second shock. As can be appreciated in this case, the ineffective ECVs maintained similar SampEn values, whereas effective attempts presented lower SampEn values and, therefore, more organized AA signals.

On the other hand, the AA organization increase (SampEn decrease) was greater in those patients who main-

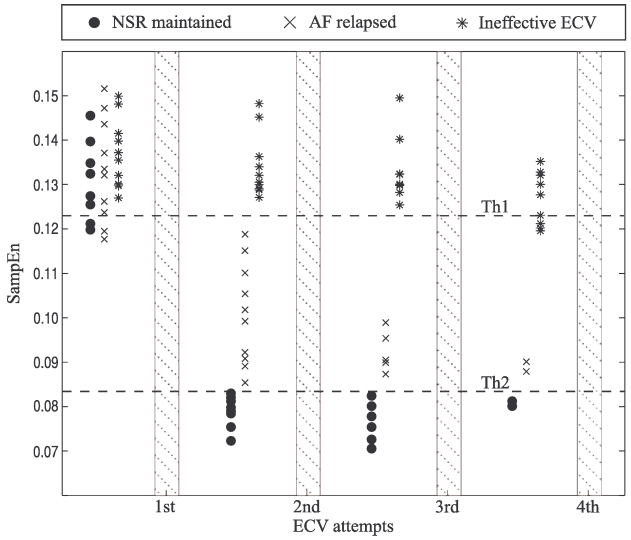

Figure 1. Analysis of the patients who needed several shocks. The MAW SampEn values obtained for the ECG segments preceding each ECV attempt are shown. For the case of NSR maintenance or AF relapsing, the result corresponds to the patient's status one month after the procedure. The thresholds Th1 and Th2 provide a discrimination framework that can be considered before the second shock.

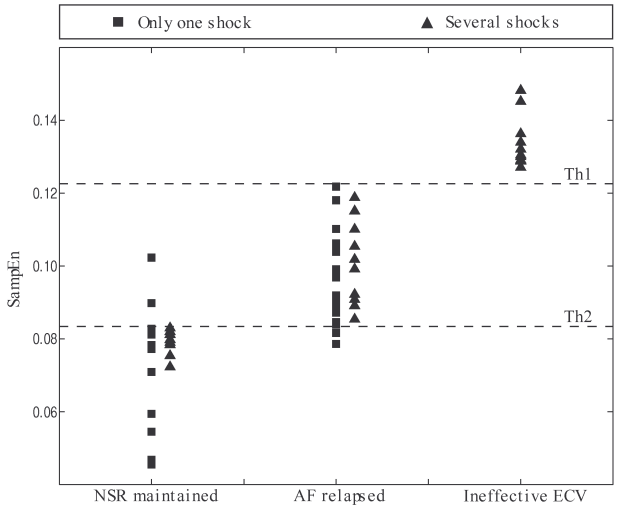

Figure 2. Classification into ECVs resulting in NSR or relapsing to AF, after one month following the procedure, and ineffective ECVs obtained with the MAW organization analysis. The SampEn values were obtained before the procedure, for the patients who only needed one shock, and after the first unsuccessful attempt, for the patients who needed several shocks.

tained NSR, after one month following ECV, than in those others who relapsed to AF. Concretely, before the second ECV attempt, SampEn values achieved a decrease higher than 33% and were below 0.0832 (Th2) for all the patients who maintained NSR. On the contrary, for the patients who relapsed to AF, the SampEn values only decreased between 20% and 28% and were between Th1 and Th2. As with Th1, the threshold Th2 was also obtained from the SampEn values estimated before the second shock.

As can also be observed in Fig. 1, after the second ECV attempt, the patients who needed additional electrical shocks presented slightly lower SampEn values and, consequently, more organized AA signals. However, the variation was notably reduced with regard to the first shock effect.

As a consequence of the results in Fig. 1 and in order to reveal some relationship between this behaviour and the patients who only needed one shock, the same method was applied to the single shock group before the cardioversion attempt. Fig. 2 shows the joint SampEn values together with the optimum thresholds (Th1 and Th2) that were obtained before. As can be appreciated, the patients from both groups who relapsed to AF presented higher SampEn values (0.0977 ± 0.0125) than those who resulted in NSR (0.0738 ± 0.0149), after one month following the procedure. Moreover, the patients in which ECV was ineffective presented the highest SampEn values (0.1341 ± 0.0072). In addition, Th1 and Th2 still may act as valid discrimination thresholds for both groups, even though they were obtained for the several shocks group. In this sense, Th1 and Th2 are statistically robust, because 91.67% (22 out of 24) of the patients who maintained NSR, 93.55% (29 out of 31) of the patients who relapsed to AF during the first month and 100% (10 out of 10) of the patients in which NSR was not restored after 4 shocks were correctly identified. In fact, the three groups were statistically distinguishable, given that statistical significances were lower than 0.0001.

4. Discussion and conclusions

In conventional ECV protocols, between 3 and 5 shocks with identical or increasing energy are delivered to the patient until NSR is restored, but the effects of unsuccessful shocks are unconsidered for delivering consecutive attempts [2]. The results obtained in this work suggest some modifications for the improvement of these protocols, which are next considered.

Comparing SampEn values computed before the first ECV attempt, for the patients who needed several shocks (presented in Fig. 1), with those obtained for the patients who only needed one shock (showed in Fig. 2), it can be considered that unsuccessful shocks are more likely in patients who present a highly disorganized AA (higher than Th1). In addition, when ECV is effective and NSR is restored, the probability of AF recurrence during the first month subsequent to the procedure is lower when the pa-

tient presents a more organized AA (below Th2). These observations highlight the fact that the higher the number of reentries wandering throughout the atrial tissue, the lower the probability of successful ECV, which has been previously reported by other authors from invasive studies [10–12].

Although an organization increase, with higher or lower proportion, was observed after every unsuccessful shock, Fig. 1 shows that the most important increase was produced after the first unsuccessful shock for the patients in which ECV was finally effective and NSR was maintained one month later. Hence, it could be considered that the first electrical shock plays the most important role in ECV and, as a consequence, in the possibility of restoring NSR after several attempts. This observation is in agreement with the results reported by two previous works where the most adequate initial shock energy was analyzed [13, 14].

Moreover, considering the effects provoked by the first unsuccessful shock, conventional ECV protocols could be improved. In this respect, if NSR is not restored after the first shock and AF organization increase is limited with a SampEn value greater than Th1 (0.1223), other shocks could be avoided because the ECV would be ineffective very likely. Regarding effective cardioversions after several shocks, the AF organization increase could reveal information about the recurrence of AF after the first month. Thus, if the SampEn value after the first shock presents a decrease greater than 33% and is below Th2 (0.0832), consecutive shocks should be delivered because ECV could be effective and NSR could be maintained, at least, during the first month. On the contrary, if the SampEn value only decreases between 20% and 28% and is between Th1 and Th2, the probability of relapsing to AF is high and, therefore, consecutive ECV attempts could be avoided for reducing patient's suffering and the consequent risks, including post–shock bradycardia, malignant ventricular arrhythmias, arterial thromboembolism and skin burns from the external paddles [2].

Acknowledgments

This work was supported by the projects TEC2007–64884 and TEC2010–20633 from the Spanish Ministry of Science and Innovation and PII2C09-0224-5983 and PII1C09-0036-3237 from Junta de Comunidades de Castilla La Mancha.

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