

Effect of atrial fibrillation organization on internal defibrillation threshold

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Summary. - Aim of the present study is to assess the effect of the organization of atrial fibrillation in the right atrium on the minimum effective cardioversion energy. Thirteen patients were studied, selected a priori for low-energy internal cardioversion (LEIC). LEIC was carried out at increasing energy levels. All patients were monitored by a multipolar basket catheter in basal condition and during cardioversion. Our results showed that the mean organization correlates with the energy of successful cardioversion, and that after each shock no significant differences (Kruskal-Wallis test) were observed in the level of organization. Similar results have been obtained for the differences of organization values, immediately before and after each shock. These results prompt for further studies aimed at measuring electrophysiological properties to predict energy thresholds.

Key words: atrial fibrillation, internal cardioversion, cardiac mapping.

Riassunto (*Effetto dell'organizzazione della fibrillazione atriale sulla soglia di defibrillazione interna*). - E' stato studiato l'effetto dell'organizzazione della fibrillazione atriale in atrio destro sull'energia minima efficace per la cardioversione. Sono stati studiati 13 pazienti, selezionati a priori per la cardioversione interna. Il protocollo di cardioversione prevedeva shock ad energie crescenti. Tutti i pazienti sono stati monitorizzati mediante catetere basket in condizioni basali e durante cardioversione. I nostri risultati mostrano che l'organizzazione media correla con l'energia efficace di cardioversione, e che non c'è differenza significativa nei valori di organizzazione dopo ogni shock. Risultati simili sono stati ottenuti per le differenze dei valori di organizzazione calcolati immediatamente prima e dopo lo shock. Questi risultati suggeriscono l'importanza di ulteriori studi sulla misura delle proprietà elettrofisiologiche per predire le soglie delle energie di shock.

Parole chiave: fibrillazione atriale, cardioversione interna, mappaggio cardiaco.

Introduction

Low-energy internal cardioversion is a widely used therapeutic approach in patients with atrial fibrillation (AF). Over the last years researches focused on reducing the energy shock by optimizing variables such as catheter position, duration and morphology of the shock waveform and drug therapy [1-3]. The reduction of the energy is particularly important in implanted devices because of the discomfort caused by the shock. Energy threshold has also been correlated to clinical and echocardiographic factors [4].

Limited attention has been paid to the investigation of the role of electrophysiological factors on the energy threshold. Two factors make these kinds of studies difficult in humans: the time required for an extensive mapping of the atria; the definition of objective measures of the electrophysiological properties of the atrial tissue.

The mapping procedure by conventional linear catheters, with 10 or 16 poles, is time consuming for the need of relocating the catheter in the various

atrial regions, in order to map a satisfactory spatial portion of the atrium. The use of a multipolar basket catheter (MBC) allows the simultaneous recording of up to 64 sites in a single atrium. It thus represents a clinically acceptable solution also in protocols consisting in repetitive shocks with increased energy.

Among various criteria introduced for classifying the intra-atrial signals during AF, the classification by Wells has gained wide popularity [5]. Other methods aimed at quantitatively estimating some electrophysiological properties of the atrial tissue during AF have been proposed [6-8]. We recently compared various methods for the assessment of the level of organization of bipolar recordings [9], according to the original classification of Wells [5].

We found that the number of occurrences, i.e. the percentage of points laying on the signal baseline, reliably discriminates the electrogram types, as defined by Wells.

Aim of this study is to investigate the effect of fibrillation organization of the right atrium on internal defibrillation threshold.

Experimental protocol

Bipolar electrograms were obtained from MBC (Constellation, Boston Scientific, MA, USA) in right atrium in 13 haemodynamically stable patients with documented persistent AF, selected a priori for low-energy internal cardioversion (LEIC). Informed consent was obtained in all cases. Antiarrhythmic drugs were suspended >5 half-lives before the study.

On arrival at the electrophysiological laboratory, all patients were in sustained AF. Patients were first monitored in basal conditions for 10 minutes. Then, a step-up protocol was used for LEIC.

Patients were adequately informed about the nature, risks and benefits of the procedure, and gave their written consent. LEIC was performed using two dedicated catheters. The first (cathode) was positioned (via femoral vein), under fluoroscopic control, in the distal part of the coronary sinus in order to embrace the left atrium as much as possible. The second (anode) was positioned in the right auricle. An additional catheter was positioned in the right ventricular apex in order to obtain satisfactory R-wave synchronization and to provide post-shock ventricular pacing. After a synchronized intracardiac ventricular electrogram was obtained, 3 ms/3 ms biphasic shocks were delivered between the two catheters by a custom-built external defibrillator (Teletronics 5410). A first shock of 50 V was delivered to confirm the integrity of the system and synchronization. Then shock energies up to 20 joules were delivered, starting with a nominal shock energy of 0.5 J, and increasing it at the following energy: 1, 2, 3, 5, 7, 10, 15 and 20 J. The procedure was stopped when a stable sinus rhythm was observed (>1 minute).

When needed, sedation was provided with midazolam starting with 2.5 mg up to a total dose of 0.1 mg/kg body weight. ECG recording was continuously performed during the procedure. All shocks were delivered on the R wave, and it was considered successful when sinus rhythm appeared within 30 s.

The MBC is composed of 64 platinum-iridium equally-spaced electrodes mounted on 8 flexible, self-expanding splines. Each spline is identified by a letter (from A to H). From the 64 electrodes, 32 bipolar electrograms were derived by combining electrodes 1 and 2, 3 and 4, 5 and 6, 7 and 8, for each spline and were labeled A12, A34, ..., H78. Details can be found in [10] (this issue).

MBC was advanced via the left or right femoral vein. Position and stability of the catheter were assessed by fluoroscopy (anteroposterior and lateral views), each minute. Bipolar electrograms were amplified, filtered (pass-band 10-300Hz), digitized (1-kHz, 16 bit) and stored on magneto-optical disk, using a Bard Labsystem polygraph. Surface leads (I, II, III, aVR, aVL, aVF and V1) were also recorded.

Measure of the organization

We focused our analysis on the level of organization, measured by the number of occurrences (NO), which has been proved to provide a reliable classification of AF organization according to Wells' criteria [9]. This parameter is computed by a real-time algorithm on each bipolar recording from the MBC, based on the estimation of the percentage number of points along the baseline, over 10-second windows. Particularly, since signal amplitude and gain may vary during the recording and differ according to channels, the data within a selected window were normalized by dividing the signal by its standard deviation. NO is defined as the percentage number of points that fall into a certain interval along the baseline. This interval was adaptively computed as follows: the amplitude range of the signal was estimated as a fraction (α) of its standard deviation (σ_x) and divided into 33 intervals (bins), with the middle bin centered across zero [11-13]. Practically, for NO estimation, only the width of the central bin (W_{bin0}) is needed. This width is thus computed as:

$$W_{bin0} = \pm 0.5 \frac{\alpha \sigma_x}{33}$$

NO is defined as the percentage ratio between the number of baseline points (i.e. points in the central bin) and the total number of points in the window. NO thus ranges between 0 and 100%. NO was calculated over 2-second non-overlapping windows. Type I AF exhibits a baseline free of perturbation and thus many points are close to the isoelectric line, yielding high NO values. Conversely, in types II and III AF the baseline is either disturbed or no longer detectable, which results in lower NO values.

The choice of α is a crucial issue: too high values of α will yield a large W_{bin0} , and bias NO toward 100; conversely, too low a values will bias NO toward 0. We set α by comparing this new method for computing NO with the one we previously validated [14]. We chose the α value which gave the best agreement between the two methods, over a set of 160 segments of type I, II and III AF. The agreement between the two methods was evaluated, as suggested by Bland and Altman [15], by plotting the differences against the mean, for various values of α . Our final choice was $\alpha = 2.975$, which gives an average difference of - 2.63%, with a standard deviation of 5.86%.

Ventricular artifact processing

Since ventricular far field artifacts (V-waves) may affect the estimation of baseline points, those electrograms points synchronous to ventricular depolarization should be excluded from NO computation, i.e. ventricular blanking. Pitschner *et al.* found that the amplitude of V-waves depends on the total

or partial prolapse of a spline into the tricuspid valve or a position near the valve circumference [16]. Ventricular blanking starts as the surface ECG derivative crosses a threshold chosen according to experimental findings (0.033 Vs^{-1}), and lasts 60 ms. NO computation is inhibited during blanking.

Effect of organization on cardioversion energy

All the electrograms were visually validated. Electrograms clearly showing poor electrode contact (i.e. low voltage, high frequency noise, baseline wandering) were removed from the analysis.

We computed NO during both basal condition and cardioversion, for each electrogram. During basal condition a global spatio-temporal average of NO (grand averaged NO) has been estimated. First, the mean NO of each region was calculated in basal condition, so as to obtain a set of up to 32 measures for each patient, averaged over the entire basal recording (10 minutes, temporal average). Then, these individual regional means were grand-averaged into one single value (spatial average).

During cardioversion, NO has been estimated 2 seconds after each shock, within a 10-second window. In addition, the difference of NO values (ΔNO) before and after each shock has been computed, according to the following formula:

$$\Delta NO = NO_{as} - NO_{bs}$$

where NO_{bs} is the NO 10 seconds before the shock (12 to 2 seconds before the shock), and NO_{as} is NO estimated within a 10-second window starting 2 seconds after the shock.

Results

The right atrium was divided in 32 anatomical regions, as indicated in [10] (this issue). The anatomical correspondence of MBC splines and bipoles with these regions have been found combining the information from the fluoroscopic projections taken during the study and from the presence of V-waves artifacts on electrograms, which are an index of the proximity of the bipoles to the tricuspid valve [17].

All the patients were successfully cardioverted, at the energy levels reported in Table 1, first column.

Table 1 summarizes the grand-averaged basal NO for each patient (mean $\pm$ standard deviation), together with the energy of the successful shock.

Fig. 1 graphically shows the results reported in Table 1. NO showed a decreasing trend: the higher the mean NO value, the lower the energy of successful internal cardioversion.

Table 1. - Averaged basal number of occurrences (NO) for each patient (mean $\pm$ SD) and energy of successful shock

Patient	Successful shock energy (J)	NO (mean $\pm$ SD) (%)
1	3	42.4 $\pm$ 14.61
2	3	28.46 $\pm$ 8.12
3	5	34.06 $\pm$ 11.85
4	7	19.78 $\pm$ 5.6
5	7	22.48 $\pm$ 9.30
6	7	28.45 $\pm$ 10.20
7	10	24.89 $\pm$ 9.43
8	15	22.87 $\pm$ 13.84
9	15	20.63 $\pm$ 7.17
10	20	20.71 $\pm$ 6.82
11	20	20.73 $\pm$ 8.04
12	20	21.34 $\pm$ 6.04
13	20	24.78 $\pm$ 6.52

Since we investigated a relatively small number of patients, we did not attempt to best fit the organization vs the successful energy level by a mathematical function. For the same reason, we did not estimate a confidence interval for the observed differences.

Fig. 2 shows the NO values after each shock, as a function of the shock energy, for one subject. For each energy level, the NO values of all the anatomical regions mapped by the MBC are reported. No region shows a trend of the level of organization when the shock energy is increased. Similar results were obtained for the other patients. Generally, after each shock no significant differences (Kruskal-Wallis test) were observed in the organization of the atrial fibrillation in the various atrial zones, for all patients. Similarly, Fig. 3 shows the ΔNO , immediately before and after each shock, for the same patient as Fig. 2. First, no significant trend characterizes the ΔNO values vs the energy (Kruskal-Wallis test). Second, ΔNO seems to randomly fluctuate spanning positive and negative values.

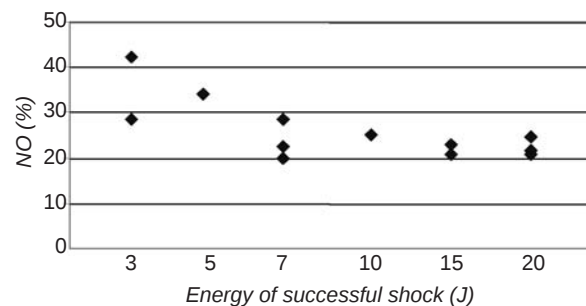


Fig. 1. - Basal number of occurrences (NO) value vs the energy of successful shock for each patient.

Table 2. - Region with maximum and minimum number of occurrences (NO) value for each patient and energy of successful shock

Patient	Successful shock energy (J)	Region with maximum NO	Region with minimum NO
1	3	PAS56	TV56
2	3	AFW12	TV78
3	5	AS12	ATV56
4	7	PAS56	ATV78
5	7	ATV12	ATV78
6	7	PFW78	TV78
7	10	TV12	ATV78
8	15	PAS56	TV12
9	15	AFW34	TV78
10	20	TV56	PFW56
11	20	LFW34	ATV78
12	20	LFW12	PLFW56
13	20	LFW12	PFW34

Also the regional distribution of the organization of each patient did not correlate to the successful cardioversion energy. Table 2 reports the regions showing the maximum and the minimum NO value, for each patient, together with the energy of successful cardioversion. No correlation exists between the cardioversion energy and either the region with the maximum level of organization or the region with minimum level of organization.

Discussion

So far, attempts to investigate the role of electrophysiological factors on the energy threshold are scarce. The time required for an extensive mapping of the atria and the definition of objective measures of the electrophysiological properties of the atrial tissue certainly contribute to make these kinds of studies difficult in humans.

Aim of this paper was to investigate the correlation between the electrophysiological properties of the right atrium during AF and the energy required for successful internal cardioversion.

Our results showed that the higher the level of organization, the lower the energy required for successful cardioversion. It has been also demonstrated by our group that the level of organization, assessed in basal condition, is stable over time and the regional disparities over the right atrium follow individual pattern rather than common distribution [10].

The several hypotheses proposed to explain the mechanisms underlying atrial defibrillation make difficult to interpret the observed correlation between successful defibrillation energy and level of organization. It has been hypothesized that the number of propagating wavefronts is related to the organization of AF [6]. If this holds true, it can be speculated that when a lower number of wavelets is involved, a lower cardioversion energy is required. Alternatively, the lower number of wavelets may reflect the higher refractory period of the atrial tissue, which in turn lowers the amount of energy required [18].

In the critical mass hypothesis the likelihood of effective depolarization depends on the ability of terminating all the propagating wavefronts [18]. As the shock strength is increased, a larger volume of the atria will experience high voltage gradients and termination of propagation is obtained. We may hypothesize that the more disorganized the atria, the higher the number of propagating wavelets, the larger the atrial volume continuing to support propagation immediately after the shock. As a consequence, the shock strength would scale with the level of organization.

Because different atrial regions shows different levels of organization, we also investigated whether the distribution of the most organized and of the most disorganized regions may explain the different energy levels required for cardioversion. On the other side, shock strength is not uniformly distributed throughout the atria.

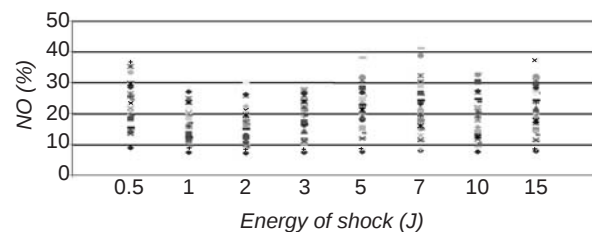


Fig. 2. - Number of occurrences (NO) values as a function of each shock, for one patient. For each energy level the NO values of all the multipolar basket catheter bipoles are reported.

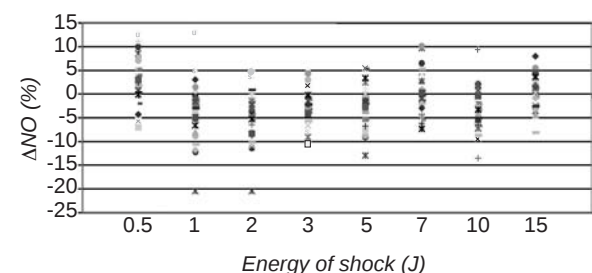


Fig. 3. - Difference of number of occurrence (Δ NO) values as a function of each shock, for the same patient as Fig. 2. For each energy level the NO values of all the multipolar basket catheter bipoles are reported.

Previous studies showed that progressive increases in shock strength caused a progressive expansion of high voltage gradients away from the shock electrodes [18]. From our data, the pattern of organization does not seem to correlate to the cardioversion energy.

We also found that no differences exist between each post-shock NO value and both basal NO and NO values immediately before the shock. One mechanism explaining the failure in defibrillating is that even though electrical activation ceases after the shock, it spontaneously regenerates within few milliseconds [18]. In addition, other studies reported that wavefront propagation was present immediately after the application of a failed shock [19]. The level of organization, when measured as NO averaged over the entire atrium, is likely expression of the organic substrate rather than of specific propagation patterns. If that is so, it is not surprising that no differences were observed in the organization immediately before and after an unsuccessful shock or in respect to the basal condition.

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