Drastic Reduction of RR Variability and Irregularity after Surgical Treatment of Atrial Fibrillation: a Comparison between Two Ablation Devices

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Abstract

Surgical treatments of atrial fibrillation (AF) create ablation lesions aiming at an electrical isolation that prevents AF initiation and maintenance. These lesions affect autonomic innervations of the atria, thus a reduction of RR variability is expected on a short and/or long period. The aim of this study is to assess the changes on variability and irregularity of RR series after ablation performed by an innovative high intensity focused ultrasound (HIFU) device, and by a classic bipolar radiofrequency (RF) device. Time and frequency domain HRV parameters, as well as Poincar plot derived indexes and entropy measure were computed before and after 12 months the operation in two groups of patients: the Study Group (SG) treated with HIFU system and the Control Group (CG) treated with RF device. Results show that after ablation, a reduction of variability and irregularity can be observed in both groups. From these preliminary results, we observed that both devices depressed post-ablation HRV on short term and long term (one year). HIFU lesions had a larger effect than bipolar RF device.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, characterized by an uncoordinated and disorganized atrial contraction, due to the existence of multiple ectopic foci. Starting from the 80s an increasing interest in the surgical treatments of AF has been registered [1]. These procedures aim to sinus rhythm restoration and maintenance, preserving atrial function and thus assuring a good cardiac performance and reducing thromboembolithic risk. The operation consists in the creation of ablation lines, usually in the left atrium and/or around pulmonary veins. These lines aim to an electrical isolation that makes the electrical depolarization follow an obligatory pathways, avoiding re-entry circuits. Ablation procedures can depress modulation of heart rate, and only moderate improvements can be observed over time [2]. Analysis of the ventricular response has been used in various studies [3, 4] in order to investigate the extent and the effects of these lesions. The aim of this study is to assess the changes on variability and irregularity of RR series using an innovative high intensity focused ultrasound (HIFU) device, and to compare it to a classic bipolar radiofrequency (RF) device

2. Study protocol

Two groups of four patients were considered in the study, conducted at the Cardiosurgery Department of the IRCCS Fondazione San Raffaele del Monte Tabor (hSR) (Milan, Italy). All patients were affected by paroxysmal AF and treated surgically with a mini-invasive ablation procedure. One group, named Study Group (SG), underwent ablation with Epicor HIFU system (St. Jude Medical) at hSR, the other one, Control Group (CG), was operated at the Groningen University Medical Center (UMCG) (Groningen, Netherlands) using a bipolar RF device (Cardioblate BP2 Medtronic). A 24-hour Holter recording was performed before and after 12 months the operation. From the ECG signal RR series were extracted by H-scribe software (Mortara Instrument). RR series were corrected from pauses, artefacts and ectopic beats, that would influence the following analysis, using linear interpolation algorithms.

3. Methods

3.1. Time and frequency parameters

Time and frequency domain indexes of ventricular response were computed following the recommendations for heart rate variability [5]. Time domain analysis includes the mean (Mean) and the standard deviation (SDNN) of all RR intervals, the root of the mean squared differences of successive RR intervals (rMSSD), the percentage of interval differences of successive RR intervals greater than 50 ms (pNN50), the standard deviation of the average RR intervals calculated over 5 minutes (SDANN), the mean of the 5 minute standard deviations of RR interval calculated over 24 hours (SDNNi). Power spectral density (PSD) was quantified using a parametric algorithms based on an autoregressive model. Three frequency bands [5] were analysed: (i) very-low frequency (VLF) from 0.01 to 0.04 Hz, (ii) low frequency (LF) from 0.04 to 0.15 Hz and (iii) high frequency (HF) from 0.15 to 0.4 Hz. In addition, the LF/HF ratio and the α-slope (slope of the line interpolating the curve log(PSD) versus log(frequency) in the VLF band) were computed.

3.2. Poincaré plot derived indexes

In the Poincaré plot, each RR interval is plotted as a function of the previous one, thus each point in the plot is given by the coordinates (RR_i, RR_{i+1}). In this way an elongated cloud of points, oriented along the line of identity at 45 degree to the normal axis, is typically obtained in normal sinus rhythm. The dispersion of points perpendicular to the line of identity reflects the level of short term variability, whereas the dispersion along the line of identity is thought to indicate the level of long term variability. These dispersions have been quantified by computing respectively the standard deviations of the points perpendicular to the line of identity (SD1) and the standard deviation along the line of identity (SD2). In addition C_{up} and C_{down} indexes, related to deceleration and acceleration of heart rate, have been calculated as follow [6]:

$$C_{up} = \frac{SD1^2_{up}}{SD1^2},\ C_{down} = \frac{SD1^2_{down}}{SD1^2} \tag{1}$$

where

$$SD1^2_{up} = \frac{1}{n}\sum_{i=1}^{nu}(D^i_u)^2,\ SD1^2_{down} = \frac{1}{n}\sum_{i=1}^{nd}(D^i_d)^2,$$

and

$$SD1^2 = \frac{1}{n}\sum_{i=1}^{n}(D^i)^2$$

where n is the total number of Poincaré plot points, nu is the number of points above the line of identity, nd is the number of points below the line of identity, D^i represents the distance of the i-th point from the line of identity, D^i_u is the distance of the ith point above the line of identity and D^i_d means the same for the points below the line of identity.

3.3. Entropy measures

Entropy is a regularity measure quantifying the randomness and unpredictability of fluctuations in a time series, as the RR intervals series. Particularly a series that contains many repetitive patterns has a relatively small entropy value, whereas a more complex and less predictable signal presents a higher value. In the present work two entropy indexes were calculated, approximate entropy (ApEn) and sample entropy (SampEn). ApEn [7] quantifies the regularity of a series as the natural logarithm of the probability that a certain pattern repeats itself in the signal. Given a sequence of length N, (RR(1), RR(2), . . ., RR(N)), and specified the pattern length m and the criterion of similarity r, two patterns, $p_m(i)$ and $p_m(j)$, are considered similar if the difference between any pair of corresponding measurements in the patterns is less than r. Considering the set P_m of all patterns of length m within the sequence, the quantity $C_{im}(r)$ may be defined as follow:

$$C_{im}(r) = \frac{n_{im}(r)}{N-m+1} \tag{2}$$

where $n_{im}(r)$ is the number of patterns in P_m that are similar to $p_m(i)$. $C_{im}(r)$ is calculated for every pattern in P_m obtaining the quantity $C_m(r)$ as the mean of all $C_{im}(r)$ values. Finally, ApEn for patterns of length m and similarity criterion r, is defined as:

$$ApEn(m,r) = \log\frac{C_m(r)}{C_{m+1}(r)} \tag{3}$$

SampEn [8] is estimated as ApEn but without considering selfmatches in the calculation of patterns recurrence probability. Values of m=2 and r=0.2 were chosen for the calculation of both ApEn and SampEn.

3.4. Statistical analysis

An unpaired, double tailed Wilcoxon test was performed for the comparison between the groups results. A p-value $<$0.05 was considered significant. A paired, one tailed Wilcoxon test was performed for comparing pre and post parameters in each single group.

4. Results

Results, reported in Table 1, show that after ablation a reduction of variability and irregularity can be observed in both groups. The mean percentage difference, one year post operation minus pre, within each group was computed and this value ($\Delta\%$) was compared between the two groups.

Figures 1 and 2 show the variation in variability assessed by time and frequency domain parameters. All the parameters, in both groups, show a negative difference related to a variability decrease after ablation. Moreover, all the parameters reductions are greater in the SG than in the CG, even if the comparison resulted statically significant ($p < 0.05$ SG vs. CG) only for the frequency domain powers.

Table 1. Absolute mean value of all the parameters ± standard deviation.

	SG (HIFU)		CG (RF)	
M [ms]	906 ± 142	767±105	928±96	787±79
SD [ms]	105 ± 16	66±11	140±38	108±27
SDANN [ms]	88 ± 14	60±8	123±37	101±28
SDNNi [ms]	53 ± 9	24±8	59±8	39±11
pNN50 [%]	9 ± 11	0.7±0.8	14±11	3±2
rMSSD [ms]	31 ± 17	13±17	41±21	22±14
VLF p [ms^2]	763 ± 198	187±114	873±236	424±254
LF p [ms^2]	349 ± 219	31±26	356±180	163±138
HF p [ms^2]	162 ± 124	19±19	246±108	52±28
Total p [ms^2]	1382 ± 414	254±170	1578±456	675±430
LF/HF	4 ± 3	3±3	2±1	3±2
α-slope	1.2 ± 0.2	1.3±0.2	1.3±0.1	1.4±0.1
SD1 [ms]	15 ± 9	6±3	20±12	12±6
SD2 [ms]	84 ± 12	55±8	107±23	89±26
Cup [%]	49 ± 2	49±2	53±2	54±4
Cdown [%]	51 ± 2	51±2	47±2	46±4
ApEn	0.89 ± 0.35	0.52±0.30	0.83±0.10	0.55±0.14
SampEn	0.73 ± 0.31	0.42±0.27	0.68±0.11	0.42±0.10

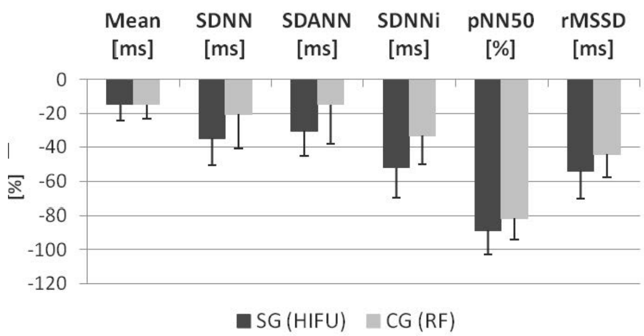

Figure 1. Mean percentage variation of time domain parameters (post 1 year minus pre) ± standard deviation.

From Figure 2, it can also be noted that in the CG the HF power is clearly the most reducted, whereas in the SG LF and HF power shows a similar reduction.

The Δ% of LF/HF ratio has opposite trends (SG: -22 ± 47, CG: 96 ± 66, p<0.05 SG vs. CG) and the Δ% of the α-slope denotes an increase of the signal correlation at the VLF particularly in the SG (SG: 18 ± 32, CG: 9 ± 8, p<0.05 SG vs. CG).

Table 2 shows the results of Poincaré plot analysis that confirm a greater reduction of variability (p<0.05 SG vs. CG), both on short and long period, in patients treated with HIFU (SG).

Finally, Figure 3 shows entropy indexes variations. Both ApEn and SampEn decrease in the two groups after the operation, highlighting signal lost of unpredictability and randomness. From the comparison between groups we can observed that SG acquires a greater RR series regularity than CG ($p < 0.05$ SG vs. CG).

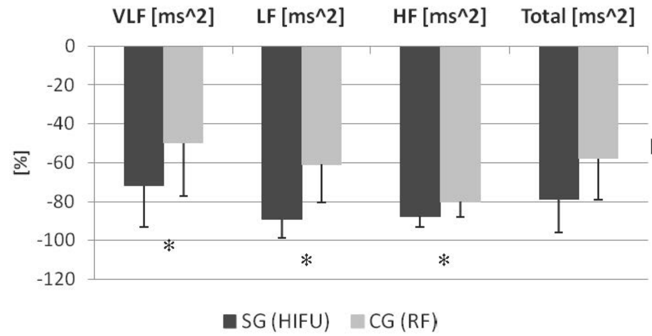

Figure 2. Mean percentage variation of specral powers (post 1 year minus pre) ± standard deviation, * $p < 0.05$ SG vs. CG.

Table 2. Mean percentage variation of Poincaré plot derived parameters (post 1 year minus pre) ± standard deviation, * $p < 0.05$ SG vs. CG.

	SG (HIFU)	CG (RF)
SD1 [ms]	-51.1 ± 20.3 *	-38.5±15.6
SD2 [ms]	-33.2 ± 14.2 *	-16.7±19.0
Cup [%]	0.3 ± 7.8	2.6 * ±6.1
Cdown [%]	0.1 ± 7.2 *	-2.8±7.1

5. Discussion and conclusions

The results obtained from analysis of RR series show, after ablation, a decrease of variability and irregularity in both groups. This confirms what previous studies have underlined, usually using time and frequency domain parameters calculated before and after different ablation procedures [3, 4]. A reduction of the autonomic nervous system control ability on the heart as well as less sensitivity of this control system, which loses its ability to reply to external stimula. It is known that a reduced variability is

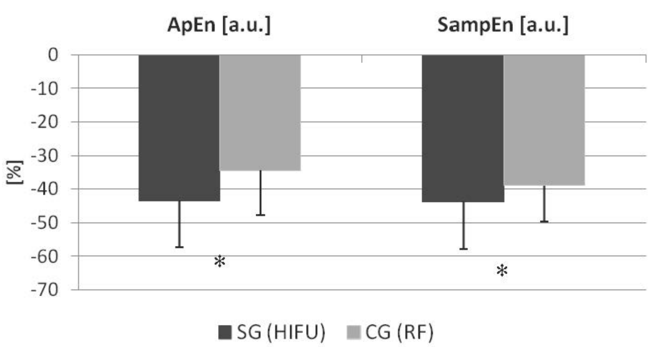

Figure 3. Mean percentage variation of entropy indexes (post 1 year minus pre) ± standard deviation, * $p < 0.05$ SG vs. CG.

linked with a lower health state of cardiovascular system. The variability decrease is, in fact, correlated with aging [9] and with the presence of specific pathologies [5, 10]. The reduction of variability and irregularity after ablation was expected [3, 4]. Obviously, the registered modifications do not have negative repercussions on the patients health. On the contrary, when the sinus rhythm restoration is obtained, patients benefit from the operation, with quality of life improvement. From these preliminary results, it seems that the HIFU lesions had a larger effect than bipolar RF device. In fact, the reduction of all variability and irregularity parameters is greater in the SG (HIFU) than in the CG (RF). Moreover, it can be noticed that, while in the RF the parasympathetic system seems to be mostly affected by the intervention, in the HIFU the ablation procedure affects the two branches of the autonomic nervous system approximately in the same way. In conclusion, from these preliminary results, it seems that ablation procedure using HIFU technology reduces drastically RR variability and irregularity.

The main limit of the study consists in the small number of enrolled patients. To obtained more reliable results, the number of patients should be increased in both group. Moreover it could be useful to evaluate a longer term follow-up, observing how the various parameters change during time.

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