Modification of the Atrioventricular Node in Patients with Chronic Atrial Fibrillation: The Role of RR Interval Distribution Pattern

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Introduction: Slowing of ventricular rate in patients with chronic atrial fibrillation (AF) and rapid ventricular response, can be achieved by radiofrequency (RF) modification of the AV node conduction. Evidence, supporting the association between the success and the failure of this method to achieve rate control and the presence or absence, respectively of dual AV node physiology, was lacking until now. However, there is evidence that the bimodal pattern of distribution of RR intervals, indicates the presence of dual AV node physiology. This study aims to evaluate the possible role of RR interval distribution pattern, as an outcome predictor of modification of AV node, in chronic AF and attempts to elucidate the likely mechanism of rate control.

Methods: Sixty-five symptomatic patients with chronic AF and rapid ventricular response (40 male, 25 female, mean age 63±8 years), in whom electrical cardioversion and medical therapy had been proven ineffective, were included. All patients underwent RF modification of AV node. Serial 24h-ambulatory ECG recordings were obtained 1 day before and 7 days, 3, 12 and 24 months after the procedure, while all anti-arrhythmic drugs were withheld. The analysis of RR interval distribution was made by means of heart rate stratified histogram technique. Exercise stress testing was carried out before and 3 months after the procedure. The follow-up period was >8 months for all pts while 63% of them were followed for >2 years.

Results: The pre-ablation pattern was bimodal (B) in 36 patients (55%) and unimodal (U) in 29 patients (45%). After the modification procedure, the B pattern shifted to U (78%) or became modified B (22%). The mean number of RF pulses delivered and the fluoroscopy time were 8±5 and 24±11 min respectively in patients with B pattern vs 18±7 and 45±17 min in patients with U pattern ($p<0.001$ for both). The location of successful ablation was posteroseptal and lower mid-septal in 26 patients (81%) with B pattern, vs 2 (13%) with U pattern ($p<0.001$). Mean and maximal ventricular rates and heart rate at peak exercise were reduced after the procedure, in both groups ($p<0.001$ for all). Long-term success rate, AV block incidence and pacemaker implantation rate were 89%, 0% and 8% respectively in patients with B pattern, vs 52% ($p<0.001$), 21% ($p=0.006$) and 48% ($p<0.001$) in patients with U pattern.

Conclusions: RF modification of AV node is expected to be more effective, safe and expeditious in patients with chronic AF and B RR interval distribution pattern. Posterior atrionodal input ablation may be the prevailing mechanism of rate control in these patients, while U-pattern patients may benefit from partial injury of the AV node.

The ideal therapy for patients with chronic atrial fibrillation (AF) who, despite pharmaceutical treatment, continue to present symptoms related to rapid ventricular response, must aim at the permanent control of the ventricular rate. It has been shown that this aim may be achieved with radio frequency catheter ablation in the posteroseptal and mid-septal region of the tricuspid annulus[1,2,3]. It has been suggested that the ablation of the "slow pathway"[1] or the partial injury of the compact segment of the atrioventricular (AV) node[2,3] may be the possible mechanisms to interpret the positive result of this method. However, since in these studies, patients suffered from chronic AF, the underlying electrophysiological properties of the AV node, both before as well as after the modification procedure, were not assessable with the standard electrophysiology study.

To date, there are no studies proving that in chronic AF, the success or failure of the AV node modification to reduce the ventricular rate, may be related to the presence or absence, respectively, of a dual node physiology. However, in chronic AF, there are data resulting from the analysis of RR interval, according to which a bimodal RR interval distribution pattern indicates the existence of a dual AV node physiology, while a unimodal distribution may be related to an orthodromic impulse propagation over the fast pathway alone[4,5]. Consequently, this study was designed to investigate the potential role of the type of distribution of the RR intervals in the clinical outcome of patients with chronic AF and rapid ventricular response, who undergo RF AV node modification.

Methods

Symptomatic patients with chronic AF and rapid ventricular response, who were to be subjected to RF modification of the AV node conduction, were considered candidates for the study's protocol on condition that: 1) all anti-arrhythmic (AA) drugs, including amiodarone, had been proven ineffective, both as far as the restoration of the sinus rhythm as well as the control of the ventricular rate were concerned, 2) the electrical cardioversion had failed to restore sinus rhythm, 3) patients agreed to stop all AA medication before the modification procedure for a period longer than 5 half-lives. Patients receiving amiodarone discontinued the drug, at least 2 months before entering the study. The exclusion criteria of the study were the following: 1) occurrence during the AA drugs weaning period of: a. symptomatic bradyarrhythmia or pause >1.5 sec, b. symptoms related to arrhythmia, without recording of ventricular rate above 100 beats / min, c) severe symptoms at rest (e.g. congestive heart failure) due to tachyarrhythmia. 2) Significant reduction of left ventricle function (EF <0.40), angina or recent myocardial infarction. 3) Thyroid disorder or other systemic diseases.

RR interval distribution type

One day before the RF modification of the AV node, all patients underwent serial 24h-ambulatory ECG recordings under conditions of usual daily activities, while all anti-arrhythmic drugs were withheld. Data were recorded on tape, while analogue data were saved in a PC (Oxford type reproduction unit). To analyze the RR interval distribution during atrial fibrillation, we used heart rate stratified histograms[6,7]. The analysis gives a uni-dimensional table that consists of all the RR intervals that have been recorded during 24 hours. Thus, this table represents the whole 24-h ECG recording. The data of this table are further analyzed in a computer as follows: 1) The table is subdivided to sequences, where each sequence includes 64 consecutive RR intervals. 2) Mean heart rate is calculated for each sequence. 3) The mean rate from each sequence is used for the organization of these sequences into groups, for every level of heart rate in a range of 10 systoles per minute (e.g. 70-80 beats/min, 80-90 beats/min., etc.). 4) For every level of 10 beats/min, we prepare a histogram of the RR intervals that belong to sequences characterized by a mean heart rate within this level. A minimum limit is required, not less than 1500 RR intervals (sufficient statistical sample). The RR interval distribution type may be unimodal, bimodal or multimodal. 5) If the distribution type is bimodal in at least two consecutive heart rate levels (e.g. 70-80 beats/min, 80-90 beats/min), the protocol will proceed as follows: In histograms presenting bimodal distribution and a maximum value less than 1000 ms, the point of section of the two RR groups is defined with visual assessment of each histogram. The RR value that corresponds to the section point is used as a division line for the separation of one RR group from the other. All those RR intervals with values below the section point are characterized as short intervals, whilst values above the section point are characterized as long intervals.

Radiofrequency modification protocol

Radiofrequency modification of the atrioventricular node was performed in all cases by the same physician who was not aware of the findings of the 24-h ECG recordings. Thus, the whole procedure was blind regarding RR interval distribution type. We had no intention to provoke atrioventricular block.

Three four-pole catheters were inserted transcutaneously and were guided under radiographic

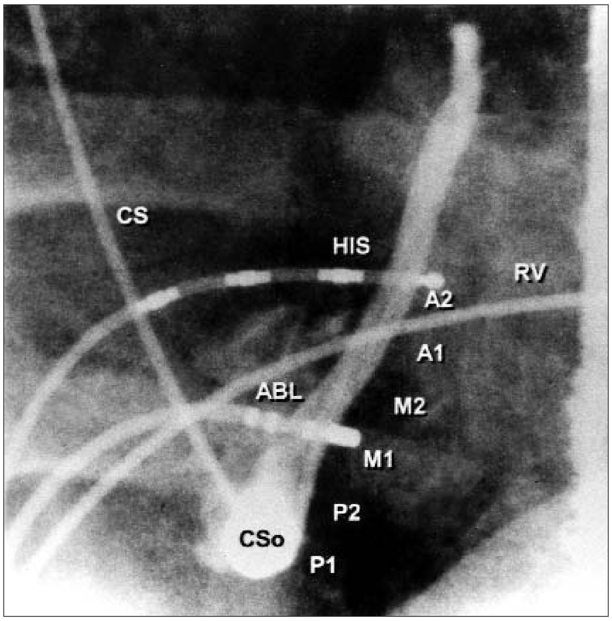

Figure 1. Coronary sinus venography in RAO 30° projection. The division of the ablation area into 6 target regions (P1-A2) is visualized. Catheters are positioned in His bundle region, right ventricle (RV) and coronary sinus (CS). ABL: ablation catheter, CSo: ostium.

guidance in the right ventricle, in the area of the His bundle and the coronary sinus. At the same time, a multi-purpose 6F catheter was inserted through the right internal jugular vein in the coronary sinus and a venography was performed of the coronary sinus, in order to determine its os. The positions of the catheter in the area of the His bundle and the coronary sinus os were recognized and depicted in a video tape in RAO 30° and LAO 45° projections, before the administration of radio frequency electricity. The ablation area from the position of His electrogram recording, up to the os of the coronary sinus was divided in two projections, in 6 equal target-points (A_2-P_1) (Figure 1). Radio frequency current, produced by a 500 KHz radio frequency generator (OSYPKA 300S), was administered between the distal end of 4 mm of a 7F guided catheter (EPT steerocath-T, EP Technologies) and one lead (7.25×1.5 in) that was placed in the left subscapular area. For each radio frequency administration, a stable electrogram recording was observed for at least 10 sec, while the ablation catheter never recorded a His bundle electrogram. In order to consider that a position is ideal for ablation, the local electrogram should present the following ratio $A_f/V < 0{,}5$.

The same radio frequency administration protocol was applied strictly in all patients as follows: The procedure started with the ablation catheter placed at the most posterior position (P1), near the coronary sinus os. If the efforts to ablate in this position were unsuccessful, the catheter would be moved consecutively forward, at positions P_2, M_1, M_2 and A_1. In each of these 5 areas, we administered 5 radio frequency pulses in total, at a position slightly different than the previous one. If, following the administration of radio frequency pulses at a specific target-position, transient reduction - mild or significant - of the ventricular rate was observed, we additionally administered 3 more pulses in this position, before we moved the catheter to the next position. With the use of a micro-processor and through an interface, we were able to measure and save the values of power, resistance and temperature. We used energy up to 50 W, for 40 sec., until the temperature of the distal end of the catheter reached 70°C. The radio frequency administration was interrupted immediately in case of increase in resistance, change of the catheter's position, abrupt prolongation of the RR interval or appearance of AV block.

The end-point of the ablation procedure was to reduce the mean ventricular rate by more than 20% and achieve less than 130 pulses/min. following isoproterenole infusion. The procedure was considered successful if the above objective had been met. The method was considered to have failed when there was no desired reduction of the ventricular rate following the completion of the protocol.

Measurement of the ventricular rate

1) During the 24-h ECG ambulatory recording, we calculated the mean, maximum and minimum heart rates, 2) During the symptom-limited exercise test, we calculated the maximum heart rate. In all cases, these rates were measured in the absence of AA pharmaceutical treatment, both before, as well as after the modification procedure.

Follow-up

Following the modification procedure, patients were hospitalized for 24 hrs in the ICU. Seven days after the operation, we proceeded to 24-h ambulatory ECG recordings that were repeated after 3, 12 and

Table 1. Clinical characteristics of the 65 patients divided into Bimodal and Unimodal Pattern-Group.

Characteristics	Bimodal Pattern (n=36)	Unimodal Pattern (n=29)	P	Total (n=65)
Age, yr	64±8.9	62±6.7	NS	63±8.1
Range	40-75	52-73		40-75
Male sex	22(61%)	18 (65%)	NS	40(61%)
Duration of symptoms, yr	3.8±2.6	4.3±2.8	NS	4.1±2.9
Type of heart disease				
None	12(33%)	9(31%)	NS	21(32%)
Coronary artery disease	5(14%)	2(7%)	NS	7(11%)
Dilated cardiomyopathy	5(14%)	5(7%)	NS	10(15%)
Valvular	4(11%)	3(10%)	NS	7(11%)
Hypertension	10(28%)	10(34%)	NS	20(31%)
Left ventricular ejection fraction, %	54±5.7	56±5.1	NS	55±5.3

24 months, during follow-up. Exercise stress testing was performed 3 months after the procedure.

The duration of the follow-up period for all patients was no less than 8 months, while 63% of the patients were followed-up for more than 2 years.

Statistical analysis

The data are expressed as mean value ± SD. The comparison between continuous and category variables was done with the "student's t-test" and the chi square method. Comparisons between the two groups, during the follow-up period, were effected with the "uni-directional" procedure, ANOVA with Bonferroni transformation. Significance was set at the level of $p<0.05$.

Conclusions

Patients' characteristics

Between June 1996 and November 1999, from a total of 133 patients with AF who underwent AV node modification, 65 fulfilled the inclusion criteria of the study protocol. Among them, 40 were men and 25 women, with a mean age of 63±8 years (range 40-75 years). The mean duration of the symptoms was 4.1±2.9 years (range 3 months - 19 years). Before the modification procedure, there was a mean number of AA drug treatments (3.7±1.6) that were proven ineffective as far as restoration of sinus rhythm or control of ventricular rate. All patients had an ejection fraction above 0.50, except 13 patients, whose EF was between 0.40 and 0.49. Twenty-six patients were on thiazide diuretics and 9 patients were on conversion enzyme inhibitors, the doses of which were maintained stable during the study.

Analysis of 24 hour RR intervals showed that 36 patients (55%) had a bimodal distribution of RR intervals, while 29 patients (45%) presented the unimodal type. Table 1 indicates the clinical features of patients who constituted the study population.

Modification results

Following the procedure, we achieved ventricular rate control in 34 out of 36 patients (94%) with a bimodal distribution and in 17 out of 29 patients (59%) with unimodal distribution pattern (p= 0,002). Failure to achieve ventricular rate reduction was seen in 2 patients (6%) with bimodal and in 7 patients (24%) with unimodal distribution (p=0,03). Inadvertent AV block was seen in 5 patients with unimodal distribution pattern and in no patient with a bimodal type (p=0,014). In patients whom the modification procedure failed to reduce the ventricular rate (2 patients with bimodal and 7 patients with unimodal distribution), we performed AV nodal ablation at a later date and implantation of VVIR permanent pacemaker. During the early follow-up phase (within 3 months after the procedure), 2 patients from each group presented recurrence of rapid ventricular response. Of them, 2 patients (1 from each group) responded in a satisfactory way to a combination of AA drugs (propranolol 40 mg, b.i.d. and amiodarone 200 mg, b.i.d.),

Table 2. Ablation results.

Results	Bimodal Pattern (n=36)	Unimodal Pattern (n=29)	P	Total (n=65)
Acute				
Success	34(94%)	17(59%)	P=0.002	51(78%)
Failure	2(6%)	7(24%)	P=0.031	9(14%)
Inadvertent AV block	0(0%)	5(17%)	P=0.014	5(8%)
Intentional AV block	2(6%)	7(24%)	P=0.031	9(14%)
Early events				
Recurrence	2(6%)	2(12%)	P=NS	4(8%)
Sudden death	1(3%)	0(0%)	P=NS	1(2%)
Syncope	0(0%)	1(6%)	P=NS	1(2%)
Long-term				
Success	32(89%)	15(52%)	P<0.001	47(72%)
Inadvertent AV block	0(0%)	6(21%)	P=0.006	6(9%)
Intentional AV block	3(8%)	8(27%)	P=0.019	11(17%)
Permanent pacemaker	3(8%)	14(48%)	P<0.001	17(26%)

while the other two patients (1 from each group) underwent AV nodal ablation and pacemaker implantation. One patient with bimodal distribution pattern experienced sudden death on the 45th day following the procedure. The autopsy findings were compatible with acute myocardial infarction. One patient with unimodal pattern presented syncope, 3 months after the operation. The ECG showed intermittent complete AV block. Thus, as far as the long term results are concerned, the success rate in the group with the bimodal distribution reached 89% (32 out of 36 patients) and 52% in the unimodal distribution group (15 out of 29 patients), (p<0.001). Inadvertent AV block was not seen in any of the first group patients, while it was observed in 6 (21%) of the second group patients (p=0.006). Finally, a permanent pacemaker was implanted in 3 of the 36 patients (8%) with the bimodal type and in 14 of the 29 patients (48%) with the unimodal type (p<0.001). The overall success rate in a total of 65 patients was 72%, while pacemaker implantation was performed in 26% of them (Table 2).

In successful cases, the number of pulses administered ranged from 1 to 22 (mean number 8.6±5.3) in patients with a bimodal distribution pattern and from 9 to 33 (mean number 18.3±7.8) in patients with the unimodal type (p<0.001), while the mean radioscopy duration was 24.2±11.7 min (range 6-57 min) and 45±17.8 min (range 19-86 min) respectively (p<0.001), (Figure 2 A,B).

The position of successful modification was posteroseptal and low mid-septal (P_1-M_1) in 26 patients (81%) with bimodal distribution, vs 2 patients (13%) with unimodal distribution (p<0.001) and high mid-septal and anteroseptal (M_2-A_1) in 6 patients (19%), vs 13 patients (87%), respectively (p<0.001).

The location of the target-position where RF pulses administration led to high degree of AV block was mid-septal in 3 cases and anteroseptal in 3 other cases (Figure 2C).

Ventricular rate control

The mean and maximum ventricular rates in the 24-h ECG recording before the modification procedure, as well as during follow-up, in the 32 patients with the bimodal and in the 15 patients with the unimodal distribution pattern with a successful outcome are seen in Figure 3. The difference in ventricular rates between the 2 groups was not significant, neither before the procedure nor during follow-up, with the exception of the maximum ventricular rate values after 12 months. In this case, the maximum ventricular rate in the bimodal group was higher (130±14 pulses/min.) compared to the unimodal group (117±5 pulses/min.), (p<0.001). (Figure 3B). Significant reduction in the mean and maximum ventricular rate was observed in both groups, during the follow-up period, compared to the respective initial

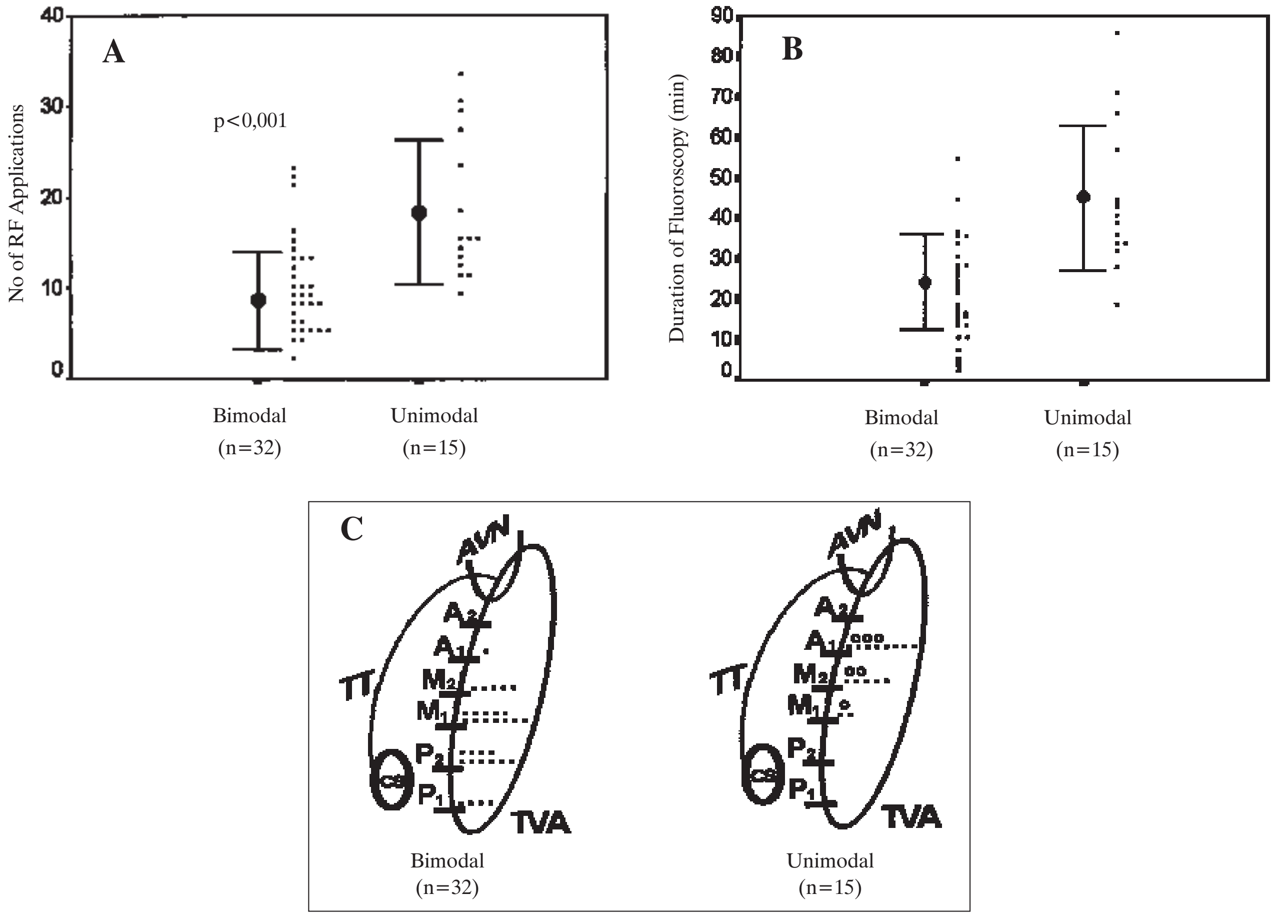

Figure 2. A statistically significant difference in the number of RF pulses (panel A) and the fluoroscopy time (panel B), was found between the 2 patterns. Panel C: The location of successful ablation in patients with bimodal (left) and unimodal (right) pattern is shown.
■: case with successful outcome after delivery of RF energy at the respective locus.
o: case of inadvertent AV block after delivery of RF energy at the respective locus.
AVN: atrioventricular node, TVA: tricuspid valve annulus, CS: coronary sinus, TT: tendon of Todaro.

values ($p<0.001$). Seven days after the procedure, patients with bimodal distribution showed 32% reduction of the mean ventricular rate from the initial value (from 111±20 to 75±11 pulses/min, $p<0.001$). This reduction was maintained without statistically significant changes throughout the follow-up period. The respective reduction in the unimodal pattern group was 30% (from 105±20 to 73±7 pulses/min., $p<0.001$) and it also remained unchanged. The reduction of maximum heart rate compared to the initial value, seen within 7 days after the procedure in patients with the bimodal distribution was 36% (from 173±27 to 110±14 pulses/min., $p<0.001$). The values of maximum heart rate in 3 months (126±15 pulses/min., $p<0.001$), 12 months (130±14 pulses/ min., $p<0.001$) and 24 months (126±11 pulses/min., $p<0.05$), were higher as compared to the value observed 7 days after the procedure (110±14 pulses/ min). The reduction of maximum heart rate, seen 7 days after the procedure in patients with unimodal distribution was 37% (from 163±22 to 103±10 pulses/min, $p<0.001$). The maximum heart rate values after 3 months (119±8 pulses/min, $p=0.015$), 12 months (117±5 pulses/min., $p=0.072$) and 24 months (120±8 pulses/min, $p=0,031$), were higher as compared to the values 7 days after the procedure with borderline statistical significance. The maximum heart rate during exercise was 190±26 pulses/min before the procedure for bimodal pattern patients and 182±19 pulses/min. for unimodal pattern patients (P=NS). Three months after the procedure, the respective values were 150±13 and 142±12 pulses/min ($p=0.058$). The duration of exercise was increased from 4.7±1.9 min to 7.6±1.7 min in patients with the bimodal type ($p<0.001$) and from 5.1±2.4

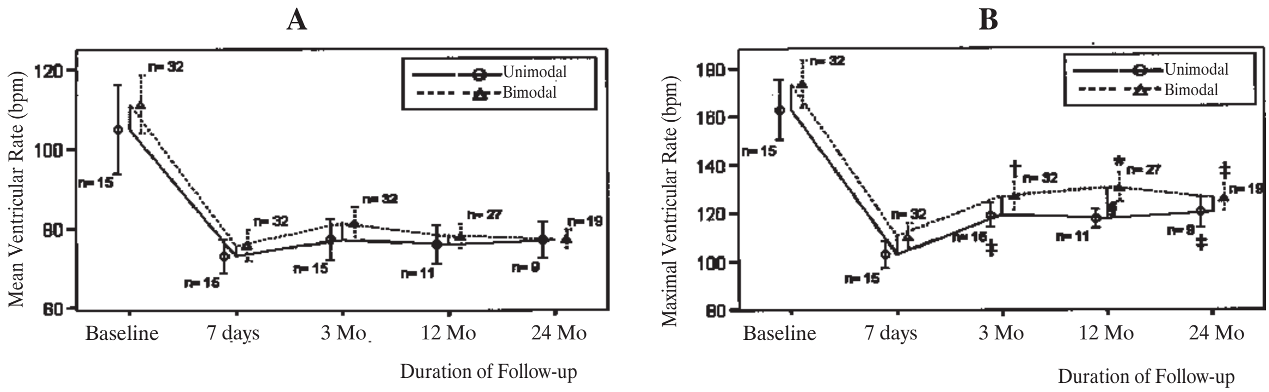

Figure 3. A. The reduction in mean ventricular rate remained without statistically significant changes throughout the follow-up period in both groups. B. Changes in maximal ventricular rate are depicted. *, P<0.001, +, P<0.01, ⁑, P<0.05, §, P<0.001. Symbols *, +, ⁑ indicate statistically significant differences between the maximal ventricular rate at 7 days and the respective rate values at 3,12 and 24 months in each group. §, indicate statistically significant difference in maximal ventricular rate between the 2 groups at 12 months.

min to 7.4±1.7 min in patients with the unimodal type, (p<0.001). All patients who underwent successful AV nodal modification remained asymptomatic or with minimal symptoms, without any need for drugs that reduce the ventricular rate.

RR interval distribution types following modification

The RR interval distribution type was assessed 7 days and 3 months after the modification procedure, in all patients with a successful outcome. In 25 of the 32 patients (78%) with a bimodal distribution pattern, the modification led to erasure of the histogram that lies on the left of the section point and represents the population of short RR intervals. Thus, the bimodal distribution pattern turned into unimodal (Figure 4). In the remaining 7 patients (22%), modification led to a shift of the section point to the right (Figure 5). In all cases where the distribution type was unimodal before the procedure, remained unimodal even after the procedure. In two patients with initial bimodal distribution pattern, who had a recurrence of the rapid ventricular rate 12 and 35 days after the procedure, respectively, a 24-h ambulatory ECG recording performed immediately after the recurrence. It is worth noting that in both patients, the first ECG recordings taken 7 days after the procedure (that is before the recurrence), presented a unimodal distribution pattern, while the post-recurrence recording showed once again a bimodal distribution pattern, similar to the one in the initial ECG recording (Figure 6).

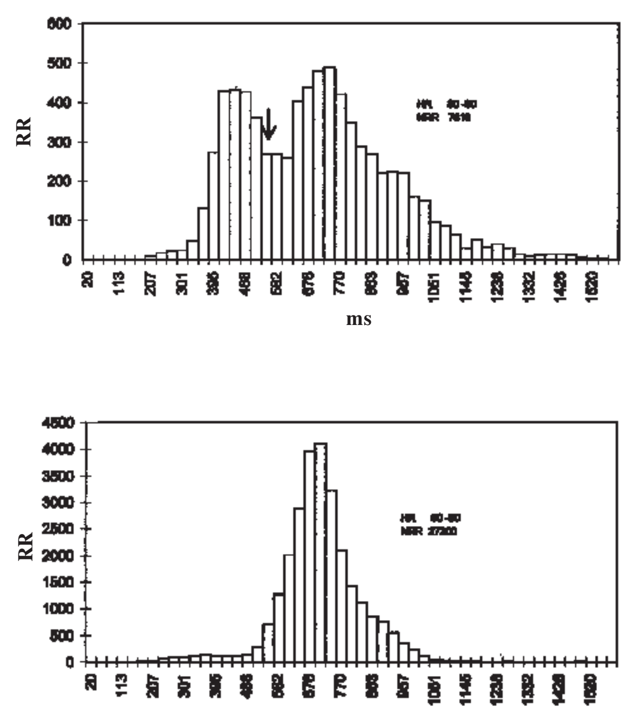

Figure 4. Upper panel. A typical bimodal pre-ablation pattern of RR interval distribution is illustrated. This RR histogram is made up of 7616 RR intervals (NRR) obtained over a 24-hour period, at an average heart rate level of 80-90 bpm. All RR intervals below the intersection of the 2 RR populations are identified as short intervals while values above this point are identified as long intervals. The intersection point (551 ms) is indicated by the arrow. ms, milliseconds. Bottom panel. After successful ablation the distribution pattern shifted to a unimodal with a substantial increase of the number of RR intervals (27.200) at the same heart rate level. However, the population of RR intervals below the value of intersection point (551 ms) has been markedly decreased.

Discussion

The ability to reduce the ventricular rate by AV node modification through radio frequency current, in patients with chronic AF and rapid ventricular response, has been reported in previous studies.[1,2] In these studies, control of the heart rate was achieved in approximately 70% of patients, while approximately 25% needed permanent pacemaker due to development of inadvertent AV block[3,8]. In our study that included similar patients population, the results are comparable to those mentioned in the above studies. Indeed, among 65 patients who were studied, overall success rates reached 72% while 26% of the patients needed a permanent pacemaker. However, when the RR intervals distribution pattern had been taken in account, before the procedure, the outcomes that resulted from the AV node modification seemed to present statistically significant differences.

The present study showed that in patients with a bimodal distribution pattern of the RR intervals, before the modification, success rates reached 94%, without any development of inadvertent AV block. On the other hand, only half of the patients from the unimodal pattern group had a successful outcome, while the other half needed permanent pacemaker implantation due to inadvertent AV block or failure of the method. It is also worth noticing that in patients with a bimodal distribution pattern, a successful AV node modification was achieved with less efforts and less radioscopy time, while the target-position for the successful administration of radio frequency current was the posterior and mid-septal area of the tricuspid annulus. On the contrary, in patients with a unimodal distribution pattern, it took almost double radio frequency pulsations and double radioscopy time, while the target-position for the successful procedure was anterior. These results signify that when AV node modification is applied in chronic AF patients with a bimodal distribution pattern, it is more likely to be successful and safe, while in patients with unimodal distribution pattern, we need more aggressive and copious procedures, with a high risk of AV block development, to achieve satisfactory control of the heart rate.

The present study showed that in 69% of the bimodal distribution patients, there was almost complete abolition of the RR short interval (shift to unimodal pattern) following successful AV node modification. This finding may indicate elimination of the posterior AV node input. On the other hand, AV node lesion does not seem probable due to the distal position of the ablation catheter from the solid segment of the AV node, the smaller number of ablation efforts and the absence of AV block. In 25% of patients with a bimodal distribution pattern who were treated successfully with AV node modification, the distribution pattern after the procedure remained bimodal, but the section point of the two RR populations shifted to the right. Thus, the new short RR intervals population that resulted consisted of “less short” cycles than those before the modification. Furthermore, it is obvious that the short RR population before the modification almost disappeared (Figure 5).

This modified bimodal distribution pattern may represent either partial injury of the slow AV node input or non-specific injury of the compact AV node, or combined modification both of the posterior as well as of the anterior atrionodal inputs. In the remaining 6% of bimodal distribution patients, the procedure failed to decelerate ventricular response. In this case, either the posterior and anterior atrionodal input may

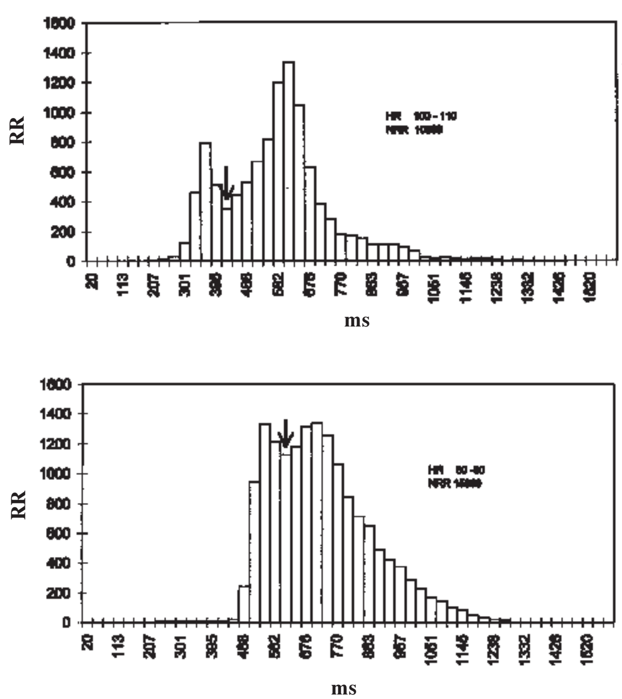

Figure 5. Upper panel. A pre-ablation RR interval histogram presenting bimodality is depicted. The value of the intersection point is 426 ms (arrow).
Bottom panel. The post-ablation RR interval histogram of the same patient is shown. The bimodality remains but the intersection point (613 ms) has been displaced to the right. It is apparent that the pre-ablation population of short RR interval (<426 ms) has been almost eliminated.

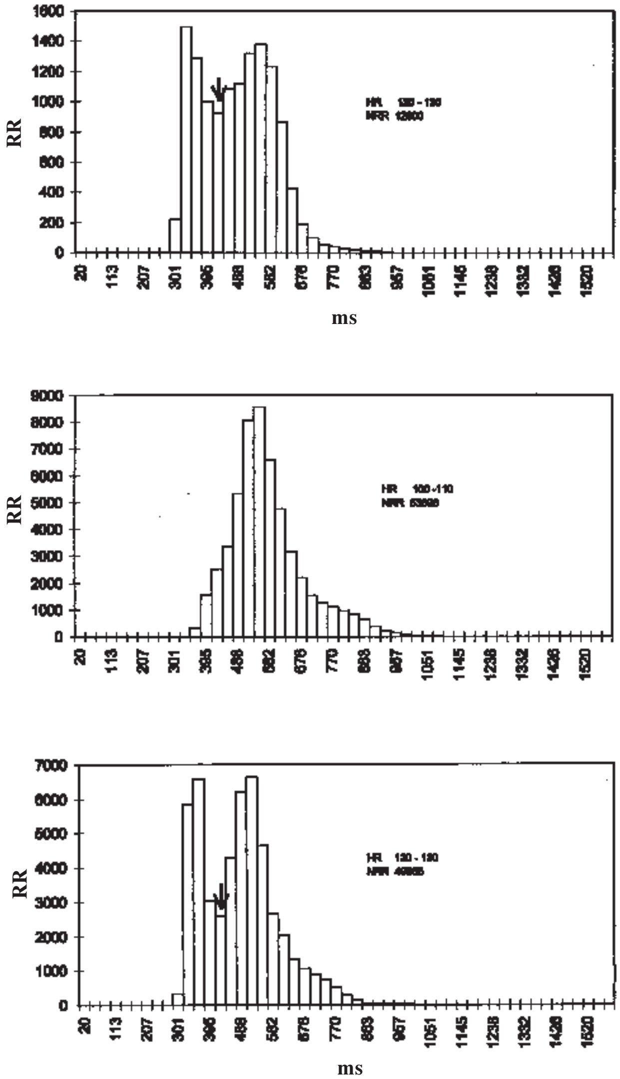

Figure 6. A bimodal pre-ablation RR interval histogram belonging to a patient who relapsed to rapid ventricular rates is illustrated (top panel). After the ablation procedure a shift from bimodality to unimodality was noted while the population of short RR intervals was almost eliminated (middle panel). Following the recurrence of rapid ventricular response, the short RR interval population reappeared and the distribution pattern became bimodal (bottom panel).

not be fully separated or the slow AV node input may be at the left atrium.

The findings of this study strengthen the opinion that the resulting RR histograms morphology does not represent a random particularity of the atrioventricular conduction but rather reflects the electrophysiological properties of a special anatomic or functional substrate, as well as the changes to which this substrate is subjected, following radio frequency administration. This theory is further enhanced by the fact that in the two cases of recurrence of rapid ventricular response, where after the modification there was a shift from the bimodal to the unimodal distribution pattern, the bimodal pattern re-appeared with exactly the same characteristics as before the modification (Figure 6). Thus, we can logically assume that the bimodal distribution pattern of the RR intervals is combined with rapid ventricular response in AF and that the abolishment of the histogram segment on the left of the section point, that is of the short RR intervals population, results in control of the ventricular rate.

An issue to be resolved is the identification of the mechanism through which a reduction of the ventricular rate was achieved in half of the patients who lack of a dual node physiology. Chen et al.[9] attributed the reduction of ventricular response following ablation in patients with paroxysmal AF without dual node to the possible presence of a posterior atrionodal input that cannot be identified with the electrophysiology study because it presents almost similar conduction properties with the anterior input or the cumulative influences from both atrionodal inputs have been destroyed, both anterior as well as posterior, after the modification[10]. Yet, in their study, the mean number of radio frequency pulsations and the mean time of radioscopy in patients without dual node physiology were much more than in patients with a dual node. Furthermore, none of the dual node patients did develop a similar late or permanent AV block, contrary to 8 patients without dual node physiology who developed it. Moreover, Krahn et al.[11] claim that half of the AF patients who undergo AV node modification may benefit from the posteroseptal ablation, without any involvement of the "fast pathway", while in the rest of the patients, the benefit may be due to a non specific injury of the AV node.

Our findings that are in concordance with data of the above-mentioned studies, suggest that the non-specific injury of the solid segment of the AV node may be the possible mechanism that interprets the benefit of unimodal patients, following modification.

Rate control

Our findings presented a trend of maintaining the degree of reduction of the maximum heart rate, during the whole follow-up period, in patients with a unimodal distribution pattern, compared to patients with a bimodal distribution pattern. This stability that was seen in unimodal pattern patients may be due to partial injury of the anterior atrionodal input, that is anyway characterized by low conduction safety factor and by a long refractory period[12]. This concept is further enhanced by the fact that the degree of deceleration of the ventricular response during provoked AF, in patients who develop AV nodal reentrant tachycardia and who undergo slow-pathway ablation, depends on the functional properties of the anterior atrionodal input[13-18].

Clinical implications

The differences that resulted in parameters such as success rates, frequency of complete AV block development, number of radio frequency pulsations administered, radioscopy time and the position for successful ablation may reflect two different types of answer in AV node modification, depending on the RR intervals histogram morphology. Thus, patients with chronic AF and rapid ventricular response who present a bimodal RR intervals distribution pattern may be the most suitable candidates for RF AV node modification. On the contrary, patients with the unimodal distribution pattern seem to be rather unsuitable and maybe they should be referred from the start for complete ablation of the AV node junction and pacemaker implantation.

Limitations of the study

Despite the detailed delineation of the AV node junction and the division of the ablation area in 6 target-regions, the exact anatomical limits of the AV node solid segment are not clearly determined[3,19-21]. Thus, for patients with a bimodal distribution pattern of the RR intervals, it is not feasible to determine if and to what extent the pulsation-mediated injuries have affected only the posterior atrionodal input, while we cannot safely exclude some degree of injury to the solid AV node.

A second limitation arises from the fact that the RR interval distribution analysis does not provide 100% accuracy in the detection of a dual node morphology, thus a unimodal distribution pattern may be combined with a "dual node physiology" of the AV node[7].

Although we recognize the limitations of this study, we still believe that the significance of our findings supports the idea that RF AV node modification may be used safely and efficiently in patients whose RR interval distribution pattern is bimodal. However, further clinical research is required to assess the clinical outcome and clarify the mechanism that explains the positive result in patients with chronic AF who undergo AV node modification for ventricular rate control.

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