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"Cardioneuroablation" — new treatment for neurocardiogenic syncope, functional AV block and sinus dysfunction using catheter RF-ablation

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functional atrioventricular block

Abstract Cardiac neuroablation is a new technique for management of patients with dominantly adverse parasympathetic autonomic influence. The technique is based on radiofrequency (RF) ablation of autonomic connections in the three main ganglia around the heart. Their connections are identified by Fast-Fourier Transforms (FFTs) of endocardial signals: sites of autonomic nervous connections show fractionated signals with FFTs shifted to the right. In contrast, normal myocardium without these connections does not show these features. RF-ablation is thought to inflict permanent damage on the parasympathetic autonomic influence because its cells are adjacent to the heart whereas sympathetic cells are remote. Twenty-one patients with a mean age of 48 years, neurally mediated reflex syncope in six, functional high grade atrioventricular block in seven and sinus node dysfunction in 13 (there is overlap between the second and third groups) were treated. Follow-up for a mean of 9.2 months demonstrated success in all cases with relief of symptoms. No complications occurred.

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Introduction

Several clinical conditions comprise transitory or permanent autonomic dysfunction by increasing vagal action and reducing sympathetic drive. As a consequence, transitory or permanent, symptomatic or asymptomatic sinus bradycardia and pauses or transient atrioventricular (AV) block may occur. The most typical examples are the cardio-inhibitory or mixed neurally mediated reflex syncope, functional transitory AV block, sinus node dysfunction and the carotid sinus syndrome. Despite having apparently normal hearts these patients may be very symptomatic and refractory to conventional medication. Consequently they represent a difficult problem for the cardiologist and many of them are referred for permanent pacemaker implantation.

Despite the fact that the pacemaker has been used as the last resort in treatment of malignant neurally mediated reflex syncope [1—4] the decision is uncomfortable in a young patient with an apparently normal heart. Furthermore, recent study has shown that cardiac stimulation may not solve all the cases with this condition [5].

Several studies have shown that a great number of parasympathetic efferent fibres and autonomic ganglia surround the sinus and AV nodes regions [1—3]. We hypothesized that a large amount of the efferent parasympathetic innervation might be eliminated by endocardial catheter RF-ablation in these areas allowing a cure or clinical control of these conditions. In this case the main challenge is to develop a safe method to locate the entry of vagal fibres into the atrial wall.

Objectives

1. Describe a method to identify the parts of the atrial wall with high density autonomic innervation;
2. Show that RF-ablation of these regions may result in sufficient parasympathetic denervation to be useful for clinical control of neurocardiogenic syncope, functional AV blocks and sinus node dysfunction.

Background

The functional bradyarrhythmias considered in this study comprise transient or persistent sinus bradycardia or AV block in the absence of evident cardiac pathology and being corrected by atropine. Clinically they present as sinus bradycardia, AV blocks, cardio-inhibitory or mixed neurocardiogenic syncope and carotid sinus syndrome being mediated by parasympathetic effect increase. Reduction of sympathetic tone may also occur. In basal conditions there is an important parasympathetic effect, the withdrawal of which causes significant heart rate augmentation as may be seen by the administration of atropine.

Cardiac autonomic nervous system

Parasympathetic

The preganglionic fibres are located in the medulla oblongata at the vagus nerve dorsal nuclei. Via the vagal nerves impulses pass to the cardiac wall where they connect with the postganglionic cells whose fibres are very short because their cell bodies are located in the atrial wall or in the para-cardiac ganglia [6—10]. The atria receive much more cholinergic innervation than the ventricles. The cardiac parasympathetic effect reduces automatism, excitability and conductivity. Contractility is less reduced because of the small number of parasympathetic vagal fibres in the ventricles.

Parasympathetic ganglia

Most postganglionic parasympathetic cells are located outside the atrial wall in the ganglia related to the atria or great vessels. Animal studies have shown three main parasympathetic ganglia located in para-cardiac fat-pads [10].

1. Ganglion A, located between the superior vena cava and the aortic root just above the right superior pulmonary vein;
2. Ganglion B, located between the right superior pulmonary vein and the right atrium; and
3. Ganglion C, located between the inferior vena cava and the right/left atrium.

Ganglion B gives most of the cardiac parasympathetic innervation. Ganglion C gives origin to the main part of the AV nodal innervation. Most of the vagal efferent cardiac fibres pass through ganglion A and thence to ganglia B and C. Only a few efferent fibres directly enter the B and C ganglia. Therefore, it is feasible to achieve parasympathetic denervation by ablating ganglion B and AV nodal denervation by ablating ganglion C. However, ablation of ganglion A provides additional and significant sinus and AV node denervation.

Sympathetic

The efferent sympathetic cardiac nervous system comprises at least two long fibres travelling away from the spinal cord to the heart [11]. The preganglionic cell body is located in the spinal cord intermedio-lateral horn. Its axon reaches the spinal cord by the anterior root and the paravertebral ganglion. The para-vertebral sympathetic chain contains the postganglionic sympathetic neurones. Their axons travel through the cardiac nerves (four or five slender branches on each side), which emerge from the three inferior cervical and from the four superior thoracic sympathetic ganglia. The fusion of the cervical inferior and thoracic superior ganglia forms the "stellate ganglion". The noradrenaline released from the sympathetic postganglionic fibres increases all cardiac properties: automatism, excitability, conduction and contractility.

Hypotheses

Considering the cells of the postganglionic parasympathetic fibres to be located in the atrial wall or in the para-cardiac ganglia we hypothesized that it would be possible to treat functional bradycardias by endocardial catheter RF-ablation. It could provide some degree of permanent parasympathetic denervation by eliminating the postganglionic parasympathetic cells. The main challenge would be to map these fibres on the endocardial wall. Therefore, we had to develop a method to detect the endocardial points of high innervation density.

Mapping the innervation on the endocardial atrial wall

By studying the spectrum of the endocardial potentials by Fast-Fourier Transformation (FFT) we have found two kinds of atrial myocardium: the *compact* and the *fibrillar* [12]. The former presents a homogeneous spectrum with one main frequency around 40 Hz and uniform conduction resulting from a mass of very well connected cells. The latter presents a heterogeneous and coarse segmented spectrum with several fractions having frequencies higher than 100 Hz shifting its FFT to the right, Fig. 1. The composition is of cell bundles working as a cluster of filaments.

Most of the parasympathetic fibres enter in the atrial wall [13]. We have observed that the nervous fibres mixed with myocardial cells changes the myocardial conduction from the compact to the *fibrillar pattern*, Fig. 2. In absence of cardiopathy we have found the *fibrillar* spectrum mainly in the sinus and in the AV node areas but it may also be found in several other places mostly in the regions near the three para-cardiac ganglia, Fig. 3. In this study the endocardial *fibrillar pattern* was used as a marker of the neuro-myocardial interface.

Methods

The study population consisted of 21 patients [4 F, 17 M] with mean age 47.5 ± 16 range 19—70 years, presenting symptomatic functional bradyarrhythmias (palpitations 10, dizziness 16 and syncope 7). There was no significant structural cardiopathy (ejection fraction $= 0.63 \pm 0.4$). The diagnoses were neurally mediated reflex syncope 6, intermittent high degree AV block 7 (three of them occurring during sleep) and sinus dysfunction 13: (brady-tachycardia syndrome in 9). All the patients were exhaustively studied by Holter, tilt-test, stress-test, conventional EP study and by atropine test permitting the functional bradyarrhythmia diagnosis.

After obtaining written consent the procedures were performed under general anaesthesia controlled by system Dräger Cicero EM. The vital signs (heart rate, oximetry, blood pressure, plethysmography, peripheral perfusion, capnography and respiratory gases) were monitored by Merlin Agilent/Philips polygraph. Brain function was monitored by BIS Aspect A-1000 keeping the conscious level between 40 and 50 bi-spectral index. The cerebral oximetry was measured by frontal infra-red spectroscopy (NIRS-Cerebral Oxymetre Somanetics-INVOS) keeping the $sRO_2 \geq 75\%$ of the pre-induction levels. After having reached the anaesthetic level (BIS index between 40 and 50) a transoesophageal echocardiogram was performed to exclude intra-cardiac thrombus and to guide transseptal puncture. The conventional EP leads were placed and a routine EP study was carried out. Heparin (5000—10,000 IU) was used to maintain the activated coagulation time around 250 s. All the patients were treated in sinus rhythm undergoing spectrally and anatomically guided ablations using a 4 mm catheter (EPT-Blazer) with the thermo-controlled system Biotronik MDS.

Spectral guided ablation

Spectral mapping was obtained on a conventional 32-channel EP polygraph (TEB-32), with specific customized software for spectral analysis (Pachón-TEB2002). A special pre-amplifier was assembled to obtain on-line spectral analysis using the software Sigview 1.9. Simplified spectral analysis was performed by means of specific three band-pass

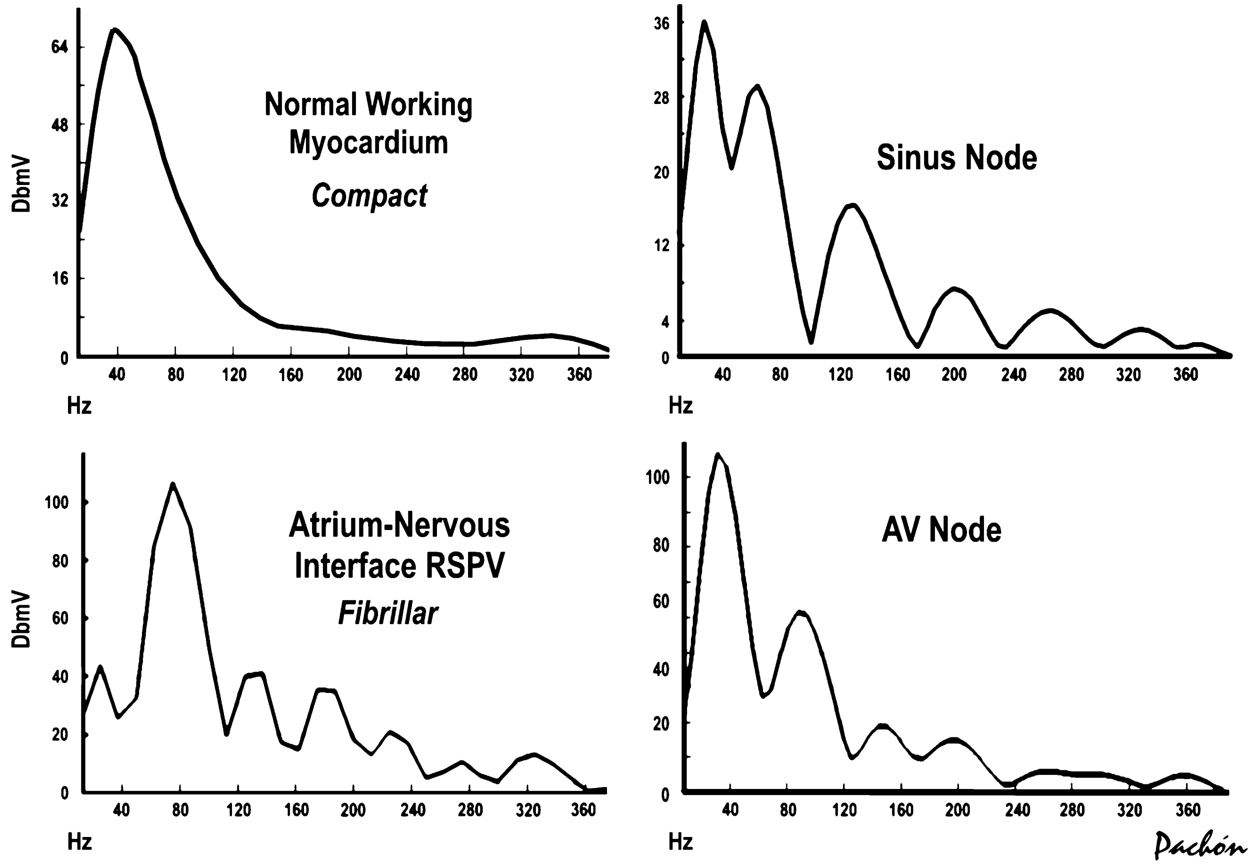

Figure 1 Spectra obtained from four endocardial sites in the left and right atria. The working myocardium (compact) registered in this case in the LA roof presents a homogeneous spectrum with main frequencies at 40 Hz in this example. All the other examples are showing fibrillar patterns with fractionated spectra and important frequencies shifted to the right such as the atrium—nervous interface observed near the insertion of the right superior pulmonary vein (RSPV). This is the typical spectrum we have sought for cardioneuroablation. It is important to remark that the sinus and AV node regions present a typical fibrillar pattern. Probably this is because of the very close relation of these structures with the nervous system.

filters with the conventional polygraph (30—500 Hz, 100—500 Hz and 300—500 Hz). In this way, studying the potentials over 100 Hz and 300 Hz, an excellent correlation was achieved with the on-line spectral analysis, Fig. 1. Thermo-controlled RF was applied, limited to 30 J, to all the points having fractionated and right-shifted spectra. Near the pulmonary veins 60 °C/15 s was used. Other points were treated with 70 °C/30 s or until elimination of the fractionated potentials above 300 Hz.

Anatomical guided ablation

Having ablated all the regions presenting segmented right-shift spectrum endocardial anatomical ablation was also performed in the regions of the epicardial fat-pads, one between the aorta and the superior vena cava (treated through the superior vena cava), the second between the right pulmonary veins and the right atrium (treated through the left atrium) and the last in the right posterior interatrial septum near the inferior vena cava (treated through the inferior vena cava and through the coronary sinus), Figs. 3 and 4. In these regions thermo-controlled RF was delivered for at least 1 min at 70 °C with 30 J maximum energy.

Immediate endpoints of the procedure

The procedures were aimed at achieving:

1. Elimination of the potentials with right spectral shift in the right and left atrial regions surrounding the sinus and AV node;
2. Persistent increase in the sinus rate;
3. Persistent increase in the Wenckebach point; and
4. Anatomical ablation.

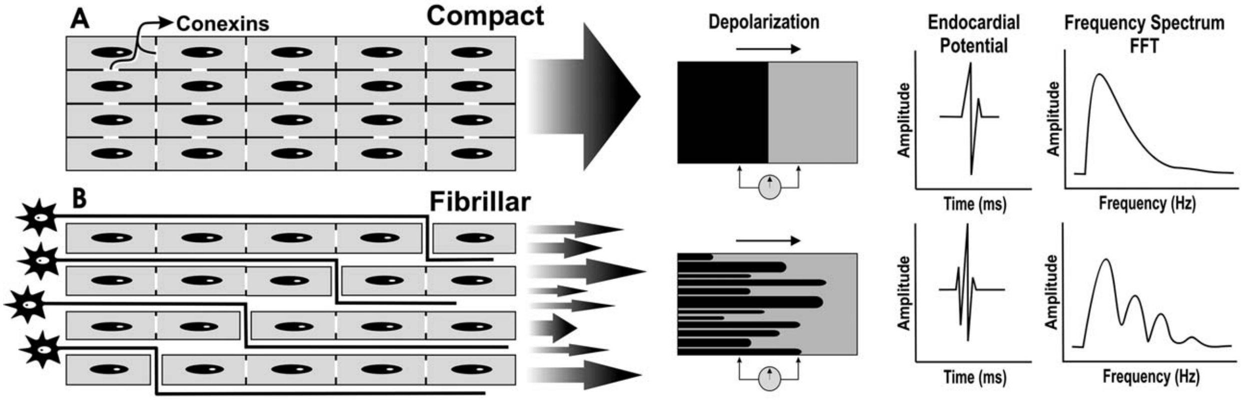

Figure 2 Schema of the interface between the autonomic nervous system and the atrial myocardium. Apparently, the penetration of the nervous fibres changes myocardial conduction and the frequency spectrum of the endocardial potential which shifts from the compact conduction (A) pattern to the fibrillar (B). The connexins are represented as small white bars between the cells. A: schema of the working normal myocardium with well connected cells (compact myocardium) that result in electrical conduction with a homogeneous spectrum; B: schema of the neuro-myocardial interface. In this point the myocardium behaves like a group of relatively independent cellular filaments because of the neural fibre interposition. It can be identified by the typical highly segmented heterogeneous spectrum with frequencies deviated to the right (fibrillar myocardium). By using specific band-pass filters it is feasible to identify both kinds of myocardium with high accuracy even in the time domain.

All the sinus and AV conduction electrophysiological parameters were measured and compared before and after the ablation. Oral anticoagulation with INR between 2 and 3 was maintained for 2 months after the procedure. All the patients having neurally mediated reflex syncope were studied again with tilt-test 1 and 6 months after the ablation. Holter was repeated at 1, 2, 6 months and at 1 year and stress-test was performed after 2 months of follow-up. The mean follow-up was of 9.2 ± 4.1 months. Statistical analyses were obtained with mean value ±SD and the Student's *t*-test for non-categorical variables. A *p*-value <0.05 was considered to be significant.

Results

All procedures were accomplished in 20 of 21 patients. In one case with an anatomical anomaly

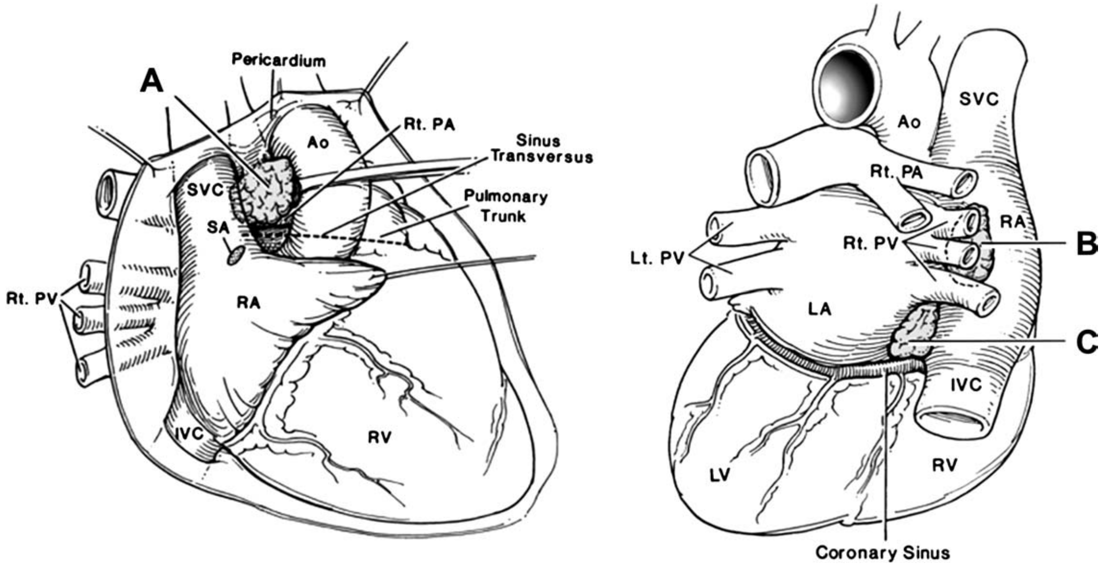

Figure 3 Schema of the para-cardiac ganglia in the canine heart according to Zipes et al. [10]. The first is located between the superior vena cava and the aorta (A); the second is located between the right superior pulmonary vein and the right atrium (B); and the third is located at the junction of the inferior vena cava, right atrium and left atrium (C).

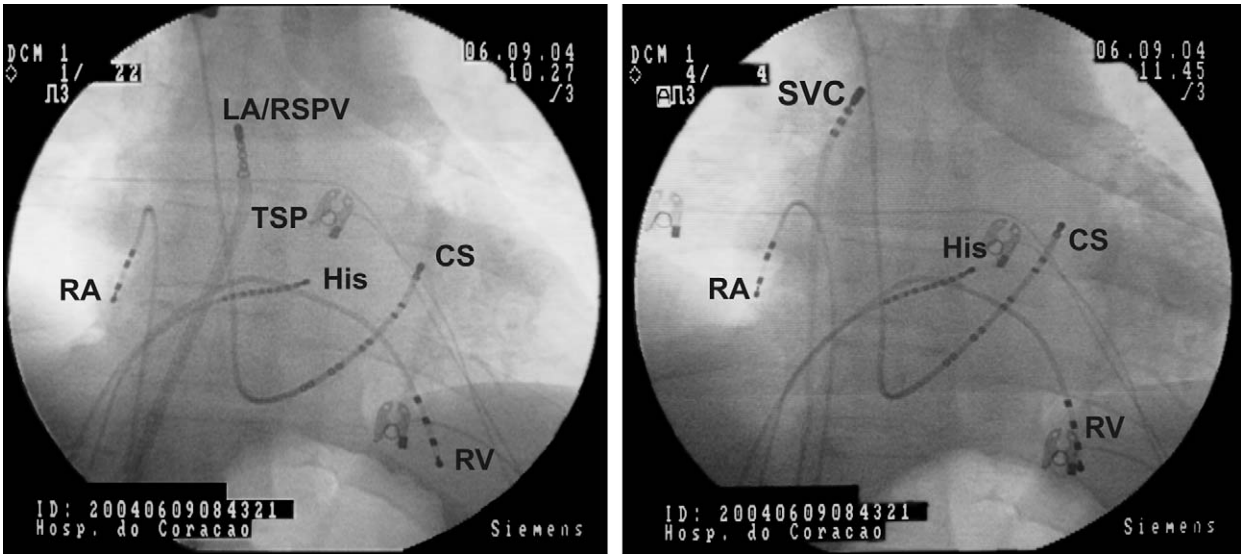

Figure 4 Methodology for anatomical ablation. The first para-cardiac ganglion is ablated on the superior vena cava medial wall (**). The approach to the second ganglion is the left atrium endocardium close to the insertion of both right pulmonary veins (*) and the C ganglion is treated by the medial wall of the inferior vena cava just below the atrium and in the ostium of the coronary sinus.

transseptal puncture was avoided due to high risk. In two cases sinus node denervation was attempted without access to the left atrium. In three cases only AV node denervation was planned by access to the right atrium. In nine cases with sinus bradycardia and episodes of paroxysmal atrial fibrillation (AF) a new technique of AF ablation was also performed based on the elimination of the ''AF-Nests'' in sinus rhythm [14]. This technique does not interfere with the *cardioneuroablation* because it is also based on right spectral shift. In the left atrium the typical fractionated right-shift spectrum was found at the insertion of the right superior and inferior pulmonary veins, in the roof and in the interatrial septum. In the right atrium, fibrillar myocardium was observed at the superior and inferior vena cava insertions, in the low portions of the crista terminalis and surrounding the coronary sinus ostium.

A mean of 28.7 ± 15 endocardial points was treated per patient. The mean fluoroscopy time was 38.9 ± 15.4 min. There were no complications.

Discussion

The possibility of promoting a definitive modification of the cardiac autonomic innervation [15] by endocardial RF catheter ablation represents a new treatment with the potential of several applications [12]. The functional bradyarrhythmias constitute an initial approach and a promising relatively safe model that could show how much can be done. It is probable that other pathologies such as the Long QT and the Brugada syndromes, ventricular arrhythmias with autonomic modulation, perhaps sleep apnoea, and other problems could be targeted by the spectral mapping and endocardial ablation in the future.

The natural model of cardiac innervation is highly suited to this approach [11,15]. The parasympathetic postganglionic neuronal cells are very susceptible to endocardial RF because they are located at (Fig. 5) or very close to the cardiac wall [9] in the para-cardiac ganglia [10], Fig. 3. The elimination of those cells makes the parasympathetic reinnervation less likely even than in cardiac transplantation [16—18]. On the other hand the cells of the sympathetic and the sensory neurones are far from the heart, Fig. 5. RF-ablation destroys only the fibres of these systems which may recover. In this case reinnervation would be much more extensive and complete than that classically observed in cardiac transplantation [19—21] because the barriers created by surgery are incomparably larger as RF-ablation causes no anatomical disarrangement.

The fibrillar myocardium areas found in this study: right pulmonary vein insertion, LA roof, interatrial septum, near vena caval insertion, intercaval space and coronary sinus ostium overlap with those of heart mammalian autonomic innervation described by Leger et al. [22] using immunoreactivity and fluorescent histochemistry techniques.

The acute autonomic denervation is very well demonstrated by the intense reduction of heart

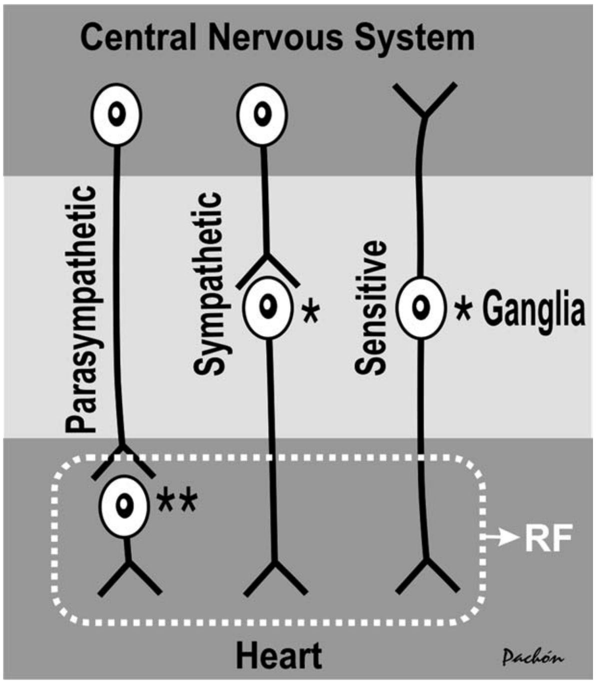

Figure 5 Schema of cardiac innervation. *Postganglionic sympathetic and sensory cells located in ganglia far from the heart; **cells of the postganglionic parasympathetic neurones located in the atrial wall or in the para-cardiac ganglia; RF: structures affected by catheter RF-ablation in the atrial wall. The parasympathetic innervation is the most affected due to postganglionic neuronal cell elimination.

rate variability observed after the *cardioneuroablation*, Fig. 6 and Table 1. Nevertheless, in the chronic phase sympathetic reinnervation is observed on the basis of recovery of the chronotropic response and by partial increase in the heart rate variability.

In this study it was feasible to obtain significant and persistent parasympathetic denervation with RF-ablation on the endocardium of the left and the right atria and in the vena cava.

The control of the ''Resting-Rate'' of the heart...

One interesting finding in this study is that on the endocardium of the left and right atria there are points presenting typical, fractionated and right-shifted spectra that cause an immediate and persistent increase in the heart rate when ablated, Fig. 7. In general they are located near the insertion of the right superior pulmonary vein and in the right atrium at the low portion of the crista terminalis. In this study the sinus rate increased 25—75% from the basal value. Endocardial potential mapping and the spectrum of this area show that these points are composed of fibrillar myocardium, probably one of the most important interfaces between the parasympathetic nervous system and the atrial myocardium, Fig. 8.

Neurally mediated reflex syncope

It can be malignant and refractory to medication resulting in serious reduction in quality of life [23]. Several different treatments have been proposed for this condition but the outcome remains less than satisfactory. Despite a pacemaker being the only option for severe cases, the VPS II trial has

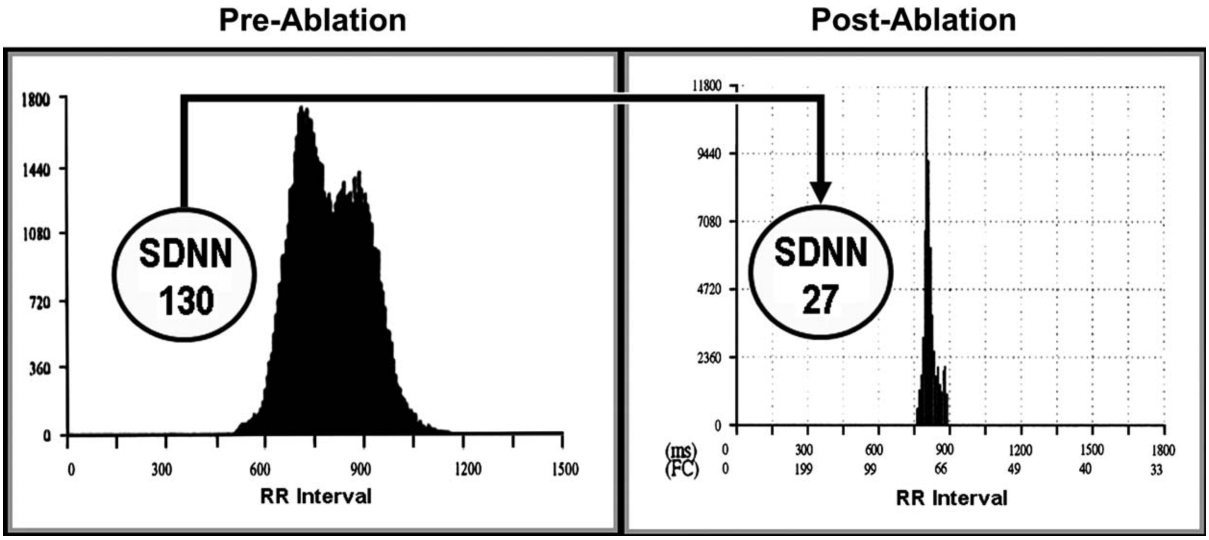

Figure 6 Heart rate variability (HRV) pre-cardioneuroablation and two-day post-cardioneuroablation of the sinus node autonomic nervous system. There is an important reduction of the HRV from SDNN = 130 ms to 27 ms showing significant decrease in the parasympathetic drive.

Table 1 Results of the *cardioneuroablation*. FU = 9.2 ± 4.1 months, A = measured at the end of the ablation procedure

Diagnostic	Pre-RF	Post-RF	*P*
Neurocardiogenic syncope 5			
Tilt-test	5/5 Positives (cardio-inhibitory)	1/5 Positive (vasodepressor)	
HRV SDNN (ms)	183 ± 42	99 ± 36 (1 month)	0.005
Syncope or dizziness	5/5	0/5 (FU)	
Functional high degree AV block 7			
Syncope or dizziness	5/7	0/7 (FU)	
AVB/Holter/24 h	High degree AVB 5/7	1 Mobitz I (sleep) 1/7 (FU)	
Episodes > 2 s/Holter	38.3 ± 56	0/7 (FU)	
Wenckebach's point (ppm)	124 ± 22	160 ± 18 (A)	0.0003
AH (ms)	87 ± 13	68 ± 18 (A)	0.004
AVRP (ms)	430 ± 83	325 ± 55 (A)	0.001
Sinus node dysfunction 13			
Bradycardia symptoms	10/13	1/13 (FU)	
Mean HR/Holter/24 h (bpm)	54 ± 7	71 ± 10 (FU)	0.0001
Minimal HR/Holter/24 h (bpm)	38.9 ± 9	50 ± 8 (FU)	0.003
Wenckebach's point (ppm)	137 ± 27	153 ± 20 (A)	0.01
Pauses >2 s/Holter/24 h	30 ± 52	None (FU)	
SNTRT (ms)	1759.6 ± 594.6	1164.8 ± 193.6 (A)	0.003
Corrected SNRT (ms)	578.9 ± 288.7	261.9 ± 97.7 (A)	0.001
HRV/24 h SDNN (ms)	183 ± 53	87 ± 13 (1 month)	0.003
Atrial fibrillation	9/13	0/13 (FU)	

shown that total protection is not provided [5]. In the present study the neurally mediated reflex syncopes were severe. One of them presented asystole of more than 30 s in the pre-ablation tilt-test. In this case the control tilt-test after the ablation presented only a vasodepressor response without syncope keeping the heart rate near 85 bpm, Fig. 9. Neither bradycardia nor asystole was observed.

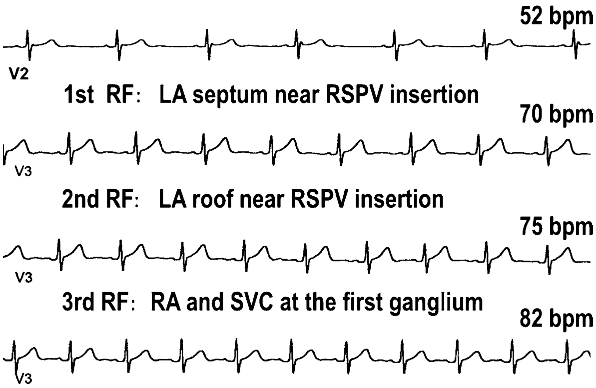

Figure 7 Progressive increase in heart rate caused by the ablation of the autonomic nervous input to the sinus node. The first two ablations were performed on the endocardium of the left atrium (LA) near the insertion of the right superior pulmonary vein (RSPV). The last was performed in the right atrium in the lateral portion (crista terminalis) and in the medial wall of the superior vena cava targeting the ablation of the first epicardial fat pad (first ganglion).

All patients show good progress in follow-up, without syncope or dizziness but they remain under close observation since it is a new treatment. Furthermore, the denervation obtained by the *cardioneuroablation* is partial having the specific aim to alter the cardiac autonomic nervous system just enough to achieve clinical control. Nevertheless the initial results and clinical outcome are highly promising. One of the possible limitations of this approach to neurally mediated reflex syncope is the specific and predominant effect on the efferent vagal fibres. Therefore, it appears that only the cardio-inhibitory response is treated, Fig. 9. In other words, the vasodepressor component cannot be treated by this method. However, elimination of cardioinhibition in the mixed neurally mediated reflex syncope may have an important part to play in the outcome.

Functional high degree AV block

Patients in this group presented high degree AV block of functional origin. They appeared mainly during sleep, disappeared on physical stress and there was no evident cardiac disease. In spite of this, four cases presented mild to moderate

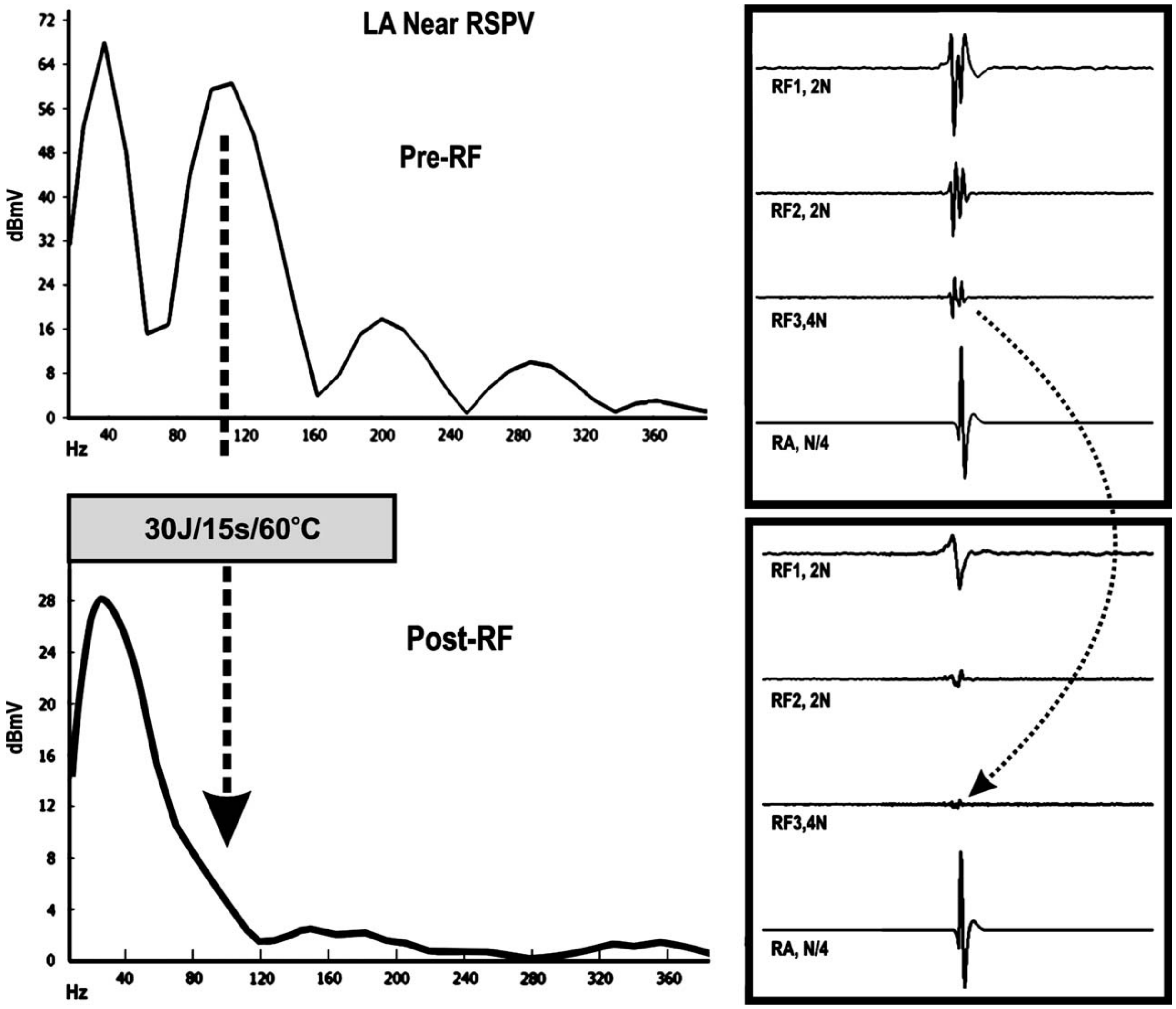

Figure 8 Example of the ablation in the left atrium near the right superior pulmonary vein (RSPV) insertion. On the left there is the spectrum pre- (upper) and post-ablation (lower). The former presents a fractionated spectrum with right-shift frequencies (fibrillar pattern). After ablation the high frequencies are nearly eliminated but the low frequencies are less affected so the fibrillar myocardium spectrum virtually changes into the compact. On the right the same phenomenon may be observed in the time domain. Filtering the endocardial signals in three channels (RF1 = 30—500 Hz, RF2 = 100—500 Hz and RF3 = 300—500 Hz) it is feasible to acquire a kind of spectral analysis. The fibrillar myocardium typically presents polyphasic signals mainly in the second and third channels. In this case even a low energy ablation was able nearly to eliminate the potentials in the third channel.

abnormalities of AV conduction electrophysiological parameters (prolonged AH interval, reduced Wenckebach point, prolonged AV refractory), which were normalized after ablation, Fig. 10 and Table 1.

In three patients the procedure was accomplished only via the right atrium. One of these patients despite having intermittent high degree AV-block pre-ablation remains with nocturnal Mobitz I AV-block post-ablation. Although this result can be considered satisfactory, by studying other cases we have perceived better nodal AV denervation when the sinus node neural input is also treated. This fact may be explained because most parasympathetic nodal AV fibres sprout from the cavo-aortic para-cardiac ganglion passing close to the sinus region [10]. Thus, we have also proceeded to sinus node denervation in all the cases we have planned a more extensive AV nodal denervation, Figs. 10 and 11. Another example came from our initial experience with one patient presenting moderate sinus pauses and very long episodes of intermittent AV block (up to 6 s) for many years. He was treated only via the right atrium aiming at AV nodal denervation. The AV block episodes were completely eliminated regardless of the nocturnal sinus pauses, which

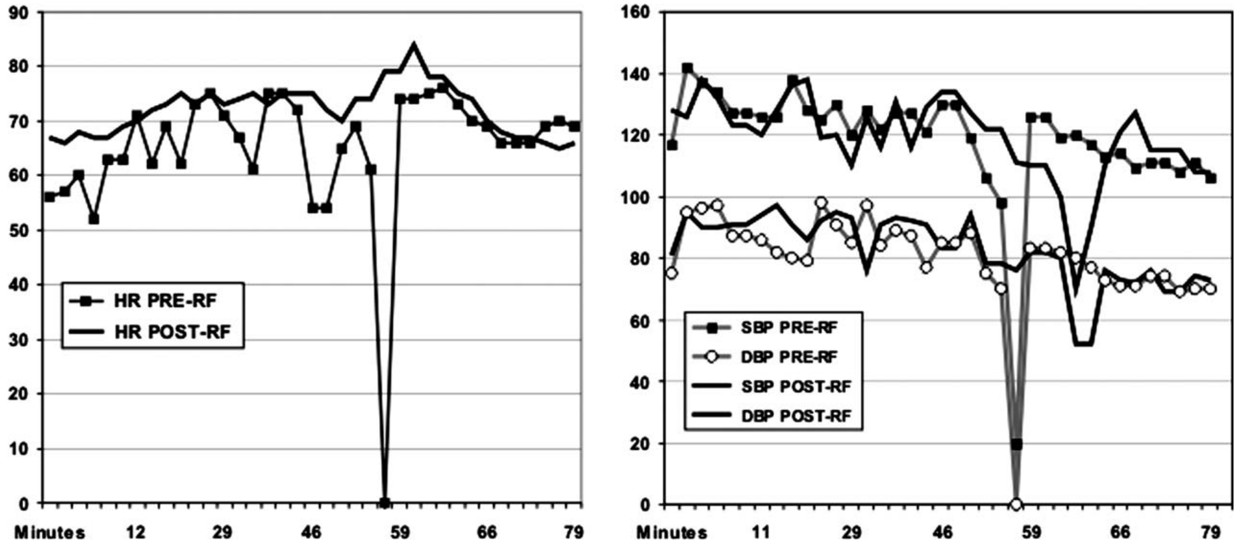

Figure 9 Even in the neurally mediated reflex syncope of the mixed type cardioneuroablation may be useful. In this case despite having not eliminated the vasodepressor response the parasympathetic denervation prevented the heart rate fall. The patient that had been presenting asystole and syncope in the first tilt-test presented only dizziness in the follow-up tilt-test. In this case, instead of heart rate fall or asystole the heart rate increased and the vasodepressor response was attenuated thus avoiding syncope.

remained unchanged. Obviously, in this case denervation of the sinus node too could have been more efficacious.

Sinus node dysfunction

This group also showed some degree of cardiopathy. The total and/or corrected sinus node recovery time was abnormal in 11 cases. However, we considered they could benefit from cardioneuroablation because of the adequate sinus chronotropic response on the stress and atropine tests. Despite having no important structural heart disease nine had brady-tachycardia, alternating sinus bradycardia with paroxysmal AF. They were also submitted to AF ablation with a new technique that does not interfere with *cardioneuroablation* because it uses the same spectral mapping without line blocks and without pulmonary vein ablation [12,14]. In this group both the bradycardia and the AF were eliminated. Hocini and Haïssaguerre et al. have observed reverse remodelling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses [24]. This finding may be related to the very extensive atrial endocardial ablations aiming at pulmonary vein isolation and line blocks that certainly cause significant autonomic denervation.

In the whole group an overall good response was observed confirmed by the control Holter that

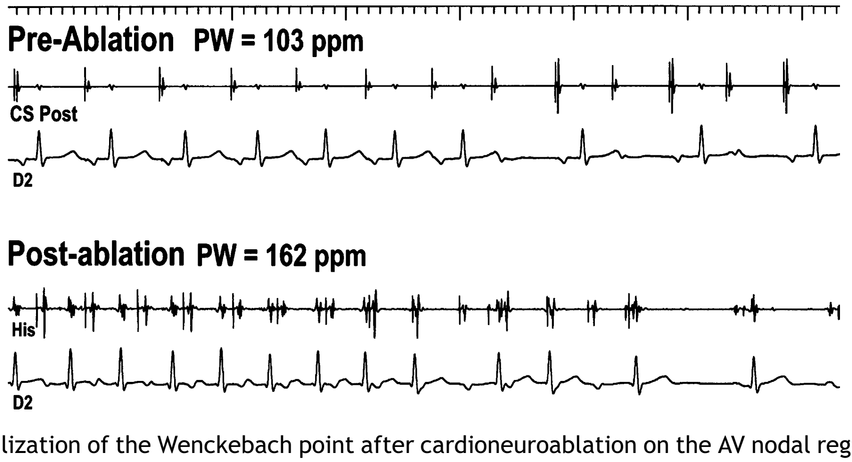

Figure 10 Normalization of the Wenckebach point after cardioneuroablation on the AV nodal region by spectral and anatomical mapping of the A ganglia.

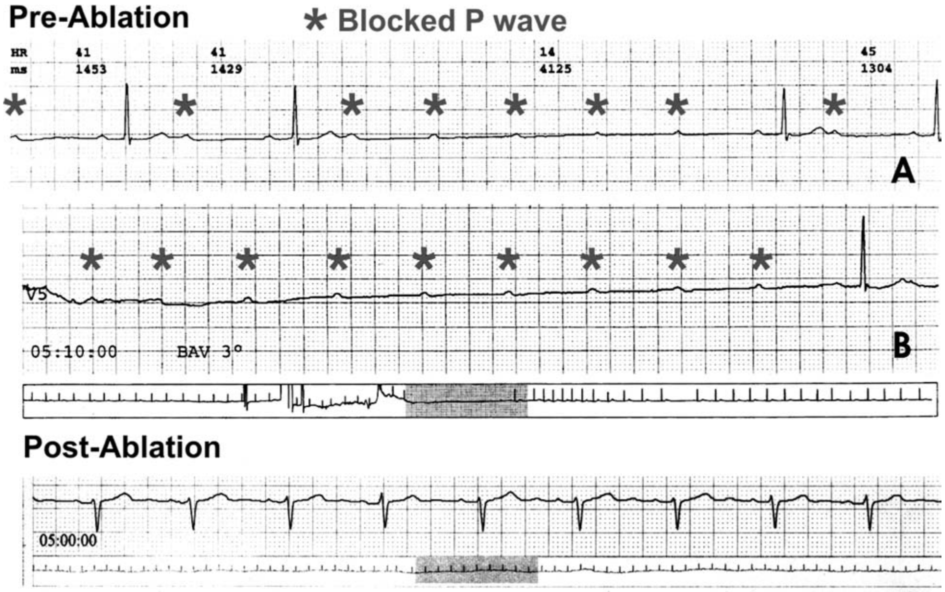

Figure 11 Holter recordings showing the 24 h lowest heart rate pre-cardioneuroablation and 2 month post-cardioneuroablation in a case of functional intermittent high degree AV block. In the pre-ablation Holter there are periods of five and nine consecutively blocked P waves. The patient was very symptomatic having syncope and dizziness being referred for pacemaker implantation. After the ablation she became asymptomatic.

showed increase in the minimum and mean heart rate (54 ± 7 to 71 ± 10 bpm), significant reduction of the heart rate variability (from 183 ± 53 to 87 ± 13 ms, $p = 0.003$), by the elimination of the pauses >2 s that previously presented a mean of 30 ± 52 in the whole group and finally by the good clinical outcome. All the patients had their sinus node recovery times normalized. These facts suggest that often, in sinus node disease it is possible to recover much of the sinus function by reducing the vagal tone, Fig. 12. In this sense this approach must now be considered in cases of sinus node disease with a pacemaker indication but a good response to atropine and without apparent cardiac disease.

Sympathetic and sensory denervation

The aim of this method was to achieve parasympathetic denervation. Lesions of the sensory

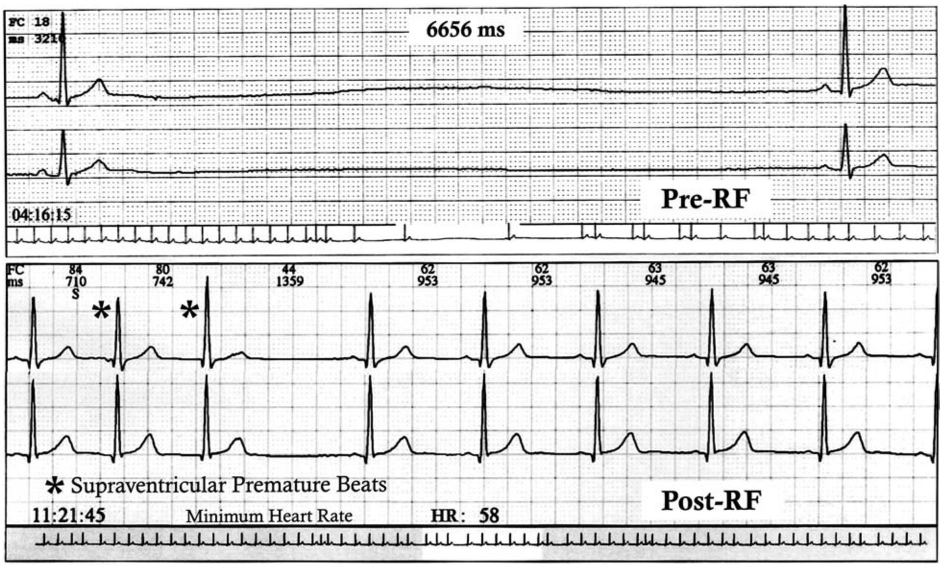

Figure 12 Comparison of the minimum heart rate pre-cardioneuroablation and 1 month post-cardioneuroablation in a case of symptomatic sinus node dysfunction without apparent cardiac disease.

and sympathetic fibres were both unavoidable and undesired. However, considering the anatomy of the cardiac autonomic nervous system only the postganglionic parasympathetic cells were eliminated by the endocardial RF-ablation. The sensory and sympathetic postganglionic cells are far from the heart and were preserved whereas the sympathetic and sensory fibres eliminated by RF have the capacity of recovery similar to that observed in post-transplantation patients [19].

Limitations of this study

Apparently there is a large variability of the autonomic nervous system caused by anatomical, constitutional and pathological factors that make it difficult to advocate one pattern approach to be applied in all the cases. Moreover this might lead to significantly diverse results.

Even when patients have a negative tilt-test its reproducibility is not enough to affirm that they are cured. Despite the very good clinical outcome long term follow-up is necessary for definitive conclusions.

The loss of chronotropic competence in the early post-ablation period may cause some exercise intolerance that progressively disappears with sympathetic reinnervation plus physical conditioning.

Obviously as we are in the ''learning curve'', the technique was not the best for all cases. There was excessive care to avoid lesions of the specialized cardiac conduction system.

Localization of the autonomic nervous entry was well defined by the spectral analysis. Nevertheless the para-cardiac ganglia ablation was based only on anatomical landmarks, which may present important individual variety. In the future, it may be possible to use specific markers from imunoscintigraphy or high precision intravascular ultrasound for very close mapping of these ganglia.

The RF deliveries for para-cardiac ganglia modification were limited in energy to avoid extracardiac injury. However, with more experience higher energy could be considered or employment of large surface or irrigated RF catheters to promote deeper lesions with higher degrees of ganglia denervation.

Despite the reproducibility and the good clinical results a larger number of patients should be treated and followed in order to allow definite conclusions.

Conclusion

The possibility of ''partial cardiac denervation'' with endocardial catheter RF-ablation may represent a new area of cardiology with a large number of potential applications. In this study we demonstrate its potential to treat functional bradycardias. The technique was easy, quite reproducible and efficient in the clinical control of the neurally mediated reflex syncope, of functional high degree AV blocks and in sinus node dysfunction, conditions which often do not present satisfactory results treated by medication and by pacing. The persistent parasympathetic denervation and sympathetic reinnervation were demonstrated by the permanent modification of heart rate variability in the chronic phase. Despite the loss of the parasympathetic the patients learned how to control cardiac rhythm mainly by modulating the sympathetic nervous system without compromising cardiac output and recovering chronotropic competence.

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