Heart Congress 2020 - Health Care Education-the New Horizon-A proposal for curriculum of preventive heart medication and healthy beating style

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Abstract

Background— Vagal incitement abbreviates the atrial successful recalcitrant period (AERP) and keeps up atrial fibrillation (AF). This examination explored whether the parasympathetic pathways that innervate the atria can be distinguished and removed by utilization of transvenous catheter incitement and radiofrequency current catheter removal (RFCA) methods.

Ages ago, medicine started in a form that is non-invasive where the symptoms were the main indicators of a dis-ease a patient complains about. This over centuries, have elevated to form the way medicine is today; the modern medicine. Truly there existed a time very recently when invasive medicine became the easy and quick resolve of medical issues—subject to approval of both the care provider and the patient. Considering the advantageous state nowadays where science has reached a point –thanks to technology advancers and to invasive-based data specialist—were the comprehensive or so called holistic medicine is by dependence on the scientific history of medicine progress has evolved into a new horizon for the new schools of medicine to come. How does the progress in the advancement of technology and the scientific consecutive revolutions affect the medical orientation by health care providers and the consciousness of the receivers of the same, on the other hand? What does medical education need to go through in order to be an easily accessible resource for individuals? How can medical knowledge be life styled to provide a strong preventive behaviour than a responsive one? What are the reflections of this on Heart Preventive Medication and Healthy Heart Life Style? This paper is designed to attend to those queries and to address the same in the conference applied to.

Conclusions—Transvascular atrial parasympathetic nerve framework adjustment by RFCA annuls vagally intervened AF. This antifibrillatory strategy may give an establishment to researching the handiness of neural removal in interminable creature models of AF and in the end in patients with AF and high vagal tone.

Note: This work is partly presented at 31st European Heart and Heart Failure Congress June on 18-19, 2020 held at Paris, France

Introduction

Parasympathetic incitement has for a considerable length of time been utilized for the acceptance and upkeep of atrial fibrillation (AF) in exploratory protocols.12 Parasympathetic incitement significantly abbreviates the atrial successful unmanageable period (AERP), in this way diminishing the frequency of atrial excitation wave fronts.3 The shorter the frequency, the higher is the likelihood that numerous reentrant circuits can exist all the while in the atrial myocardium; the nearness of these various circuits, thusly, builds the strength of AF.4 Clinical proof for a job of the parasympathetic sensory system in human AF has been given by perceptions of Coumel5 and Chen et al.6

The reason for the current examination was 2-overlap. To begin with, we wished to decide if transvascular electrical incitement with a catheter can be utilized to recognize the area of the parasympathetic nerve strands that innervate the atria. Second, we assessed the adequacy of transvascular radiofrequency catheter removal of these nerves to parasympathetically denervate the atria.

Methods

Surgical Preparations

All animal studies were endorsed by the Research and Development Committee of the Department of Veterans Affairs Medical Center, Oklahoma City, Okla. In 11 mutt hounds (18 to 23 kg), sedation was performed with sodium pentobarbital (beginning bolus 30 mg/kg IV, 50 to 100 mg varying for upkeep). The pooches were ventilated with room air (Harvard Apparatus Co). After right horizontal thoracotomy, the heart was uncovered in a pericardial support. Multielectrode catheters (Cordis Webster Corp) were stitched to one side predominant pneumonic vein, the Bachmann's pack, the privilege atrial limb (RAA), and the low right chamber (LRA). Another multielectrode catheter was embedded into the coronary sinus. Surface ECG lead II/aVR and intracardiac tracings were recorded by utilization of a Bard Labsystem (CR Bard Inc).

Parasympathetic Autonomic Nerve Stimulation

For cervical vagal nerve incitement (VNS), the cervical vagosympathetic trunks were cut, and silver wires were presented in the cranial finish of the vagosympathetic trunk. Rectangular electrical improvements were conveyed at a recurrence of 20 Hz and a heartbeat span of 2 ms (Grass trigger S-88, Astro Med Inc, Grass Instruments Division). The voltage picked for right (left) VNS was 5 V over the voltage at which sinus capture enduring >2 seconds (total atrioventricular [AV] square) was accomplished. These incitement qualities were likewise applied during respective VNS and were kept steady during the investigation.

For incitement of cardiovascular parasympathetic nerves in the privilege aspiratory supply route (RPA), a container catheter (Cordis Webster Corp, Figure 1), which comprised of a 7F shaft with an expandable bin formed anode cluster at its end, was utilized. The bushel comprised of 5 metal cathode arms. Bipolar electrical incitement could be performed between neighboring arms of the crate (incitement recurrence 20 Hz, beat length 0.1 ms; Grass trigger S-88, Astro Med Inc, Grass Instruments Division). The bushel catheter was brought into the proximal RPA under fluoroscopic direction. To distinguish an intravascular site in the RPA at which parasympathetic cardiovascular nerves could be animated, the easing back of the sinus rate during incitement over each pair of terminal arms at 35 V was estimated. This sinus rate easing back has recently been demonstrated to be intervened by parasympathetic cardiovascular nerves.7 If no recognizable rate easing back happened during incitement over each pair of splines, the container was contracted and step by step progressed or pulled back inside the RPA until a site with a noticeable sinus rate easing back was found. To determine that the incitement/removal site in the RPA was far off from the chamber, we affirmed that the atria couldn't be paced from the RPA. For this reason, pacing upgrades at cycle lengths of 400 to 500 ms were conveyed with 35 V (motivation term 2 ms) in the RPA each time before high-recurrence electrical incitement/removal was begun in the RPA.

In 2 dogs, transvascular parasympathetic incitement (TPS) was performed at the fringe of the sub-par vena cava (IVC) to the correct chamber inverse a fat cushion between the sub-par right chamber, the IVC, and the ostium of the coronary sinus. This fat cushion

has been appeared to transcendently innervate the AV hub yet additionally parts of the atria.89 Stimulation (20 Hz, beat span 0.1 ms) in the IVC energized atrial tissue, coming about in AF, which ended following suspension of electrical incitement. In any case, other than energizing atrial tissue, TPS in the IVC brought about a significant ventricular rate easing back impact during AF, as portrayed previously.10 The nearness of such ventricular rate easing back during AF was taken as a sign that the crate catheter was situated nearby the parasympathetic fat cushion.

Measurement of AERPs and AV Conduction

AERPs at 7 atrial destinations were estimated at benchmark during one-sided or two-sided VNS and during TPS in the RPA by utilization of the extrastimulus method (essential cycle length 300 ms, last extrastimulus stages 1 ms) and pacing boosts at double the diastolic pacing edge. The longest coupling span that didn't catch the atria was characterized as AERP.

To survey the heterogeneity of the AERPs, we determined the coefficient of variety of the AERP (COV-AERP=standard deviation/mean×100%) at the 7 atrial destinations in each pooch. An expanded COV-AERP has been shown to be emphatically related with atrial powerlessness to AF.11 AV conduction was assessed by steady pacing from the RAA until Wenckebach type 2 AV square happened.

Ganglionic Blockade

In 4 creatures, AERP judgments during VNS or TPS in the RPA were performed when the implantation of hexamethonium chloride (bolus infusion 7.6 mg/kg body wt, support mixture 0.76 mg/kg body wt every moment; Sigma Chemical Co), a nicotinergic ganglionic blocking operator.

Radiofrequency Current Ablation

Conveyance of radiofrequency current happened in a unipolar mode between one of the splines and a cutaneous fix cathode. On the other hand, electrical incitement of parasympathetic nerves was acted in a bipolar manner over contiguous splines of the container catheter. In this manner, with the applied catheter, we couldn't recognize a solitary spline however a couple of splines that uncovered most extreme reaction to high-recurrence incitement. For removal, radiofrequency current was first conveyed to 1 of the 2 splines of the terminal pair with maximal reaction to high-recurrence incitement. On the off chance that there was as yet a shortening of the AERP during VNS and incitement over the pair of splines of the container catheter after the principal removal endeavor, the second of the 2 splines was picked for radiofrequency current removal (RFCA). Radiofrequency current was conveyed at 520 kHz/70 V for 60 seconds (American Cardiac Ablation Corp).

Statistical Analysis

All information are communicated as mean±1 SD. AERPs and cycle lengths at which 2:1 AV nodal square happened were thought about by methods for a Student combined t test. Estimations of $P \leq 0.05$ were viewed as huge.

Results

Cervical VNS

During supramaximal reciprocal VNS, the AERP at all 7 atrial destinations abbreviated from 123±4 ms at standard to 39±4 ms ($P<0.001$, n=11). The level of AERP shortening at every one of these 7 atrial destinations is delineated in Figure 2. Respective VNS additionally expanded AERP heterogeneity as estimated by COV-AERP (9±3% without versus 27±13% with reciprocal VNS, $P<0.001$; n=11).

Transvascular Parasympathetic Stimulation

TPS in the RPA essentially abbreviated the AERP at all 7 atrial locales from 123±4 ms at pattern to 66±13 ms (P<0.001; n=11, Figure 3). TPS in the RPA additionally expanded the AERP heterogeneity (COV-AERP 9±3% at gauge versus 30±12% during TPS in the RPA, P<0.001; n=11). During TPS in the RPA, AF could be actuated with a solitary extrastimulus at every one of the 7 atrial locales and could be kept up as long as RPA incitement was proceeded. Paradoxically, without TPS in the RPA, the enlistment of AF during customized incitement was uncommon. RPA incitement likewise altogether expanded the supraventricular cycle length from 400±88 ms (n=11) at standard to 870±342 ms during TPS (n=10, P<0.001) and prompted a sinus hub capture in 1 creature. There was a critical prolongation of the antegrade Wenckebach cycle length during RPA incitement (187±24 ms at standard [n=11] versus 297±117 ms during TPS in the RPA [n=8]). In 3 creatures, TPS in the RPA caused a total AV square.

Intravenous imbuement of hexamethonium chloride in 4 canines totally annulled the AERP shortening at all 7 atrial destinations during respective VNS and TPS in the RPA (123±6 ms for standard AERP versus 53±22 ms during TPS in the RPA before hexamethonium [P<0.001] and versus 122±5 ms during TPS in the RPA after hexamethonium [P=NS]). Additionally, intravenous infusion of 3 mg atropine forestalled the acceptance of continued AF during customized incitement and respective VNS or TPS in the RPA.

In those 2 canines wherein RFCA was acted in the IVC, high-recurrence incitement in the IVC before RFCA prompted a checked reduction of the ventricular rate during AF (RR stretch was 884±392 ms with TPS versus 221±33 ms without TPS).

Effect of Transvascular Atrial Parasympathetic Nerve System Modification on AERPs

Transvascular RFCA of atrial parasympathetic nerves was acted in 7 pooches. In 4 canines, RFCA was confined to the RPA, though in 1 pooch, removal was acted in the RPA and the unrivaled vena cava (SVC). In 2 mutts, removal was acted in the RPA and in the IVC near the correct chamber. Critically, at the removal destinations in the RPA and in the SVC, electrical catch (pacing) of atrial myocardial tissue never happened and after removal even at the most elevated conceivable incitement voltage. Thus, electrical high-recurrence incitement in the RPA never prompted AF except if concurrent modified atrial incitement was performed. By and large, 9±4 RFCA with an impedance of 178±64 Ω was conveyed in every creature. The end purpose of RFCA was the noninducibility of supported AF (>20 seconds) with a solitary atrial extrastimulus during supramaximal two-sided VNS.

Intravascular RFCA of atrial parasympathetic nerves altogether decreased the AERP shortening that was expected to supramaximal respective VNS at all 7 atrial locales (Figures 4 and 5). Transvascular RFCA of atrial parasympathetic nerves additionally prompted a critical increment of the standard AERP at all 7 destinations (from 123±4 ms before removal to 127±3 ms after removal, P=0.002; n=7, Figure 4). Prior to removal, AF could be handily actuated and kept up for >1 hour at every one of the 7 atrial destinations during two-sided VNS and customized atrial incitement with a solitary extrastimulus, while after removal, continued AF was not, at this point inducible during synchronous reciprocal VNS at any of the 7 atrial locales notwithstanding forceful quick atrial burst pacing (10 seconds with 10 Hz). The heterogeneity of the pattern AERPs didn't contrast altogether before RFCA (COV-AERP 9±3%) and after RFCA (COV-AERP 8±3%).

On the other hand, the expansion of AERP heterogeneity during reciprocal VNS was nearly canceled after removal (COV-AERP during two-sided VNS was 30±14% before removal versus 12±7% after removal; P=0.02).

In 1 pooch, after removal in the RPA, an AERP shortening during two-sided and right VNS was as yet present at the RAA and LRA, and continued AF stayed inducible. In this canine, TPS was acted in the SVC, 3 cm over its intersection with the correct chamber, where an extensive abatement of the AERP at the RAA and LRA was acquired during TPS. After use of one RFCA beat in the SVC, the AERP shortening during VNS was canceled, and AF was rendered noninducible during VNS. In 2 mutts, extra RFCA was acted in the IVC. In 1 canine, the AERP at the proximal Bachmann's pack LRA still abbreviated during two-sided or right VNS, and supported AF was inducible. Utilization of 3 RFCA heartbeats to the IVC (2 current applications to a similar spline at a similar area and 1 current application to the subsequent spline) blunted this AERP shortening, and supported AF got noninducible. In the subsequent canine, left and reciprocal VNS still extensively abbreviated the AERP at the distal coronary sinus, and continued AF stayed inducible. After utilization of one radiofrequency current heartbeat to the IVC, VNS not, at this point diminished the AERP at the distal coronary sinus, and AF got noninducible.

Effect of Transvascular Atrial Parasympathetic Nerve System Modification on Sinus Rate and AV Conduction

After removal, reciprocal VNS not, at this point altogether diminished the sinus rate (AA spans were 440±123 ms without VNS versus 405±92 ms with two-sided VNS) or delayed the antegrade Wenckebach cycle length (191±31 ms with VNS and 185±28 ms without VNS). The standard sinus musicality cycle length didn't change fundamentally previously (409±102 ms) and after (440±123 ms) removal. Essentially, no noteworthy difference in the standard antegrade Wenckebach cycle length was seen previously (185±28 ms) and after (203±38 ms) removal. After removal at the IVC, the negative dromotropic impact during TPS in the IVC was canceled.

Histopathology

Plainly visible after death assessment of the removal locales in the RPA and SVC indicated straight injuries of 5 to 10 mm however didn't uncover obvious intravascular thrombi joined to these sores (Figure 6). The RFCA sores were seen as situated at the floor and the ventrolateral mass of the proximal RPA. In 2 canines in which removal was acted in the IVC, perceptible sores (length 3 to 4 mm) were seen at the back and left sidelong part of the IVC at its change to the correct chamber. Histological areas demonstrated different nerves in the stringy and greasy tissue encompassing the RPA (Figure 7). After removal in the RPA, a hemorrhagic exudate and a polymorphic invade could be seen around the nerves in the stringy and greasy tissue encompassing the RPA inverse the intravascular removal sore. Plainly visible assessment and histological assessments of the atria of mutts that were removed only in the RPA didn't uncover indications of atrial harm after the removal method.

Discussion

The current examination exhibits how the significant parasympathetic pathways to the atria can be recognized by utilization of a catheter-based transvenous approach. The outcomes further show that intravascular RFCA of these parasympathetic nerves can be accomplished; this removal totally abrogated the AERP shortening and the expanded AERP heterogeneity during reciprocal VNS and forestalled the acceptance and upkeep of AF during VNS. A careful strategy for atrial parasympathetic denervation requiring a thoracotomy was initially evolved by the intricate investigations of Kaye, Randall, and

associates 1213 and was later altered by Chiou et al.9

A few clinical perceptions have recommended that an expanded parasympathetic tone is associated with the beginning of probably a few types of paroxysmal AF.56 However, the job of the parasympathetic sensory system in incessant AF is less clear. In atrial biopsies acquired from patients with constant AF, the acetylcholinesterase movement was demonstrated to be altogether decreased contrasted and the action in patients with sinus rhythm.14 Therefore, a lower inactivation pace of acetylcholine may represent a higher vagal tone in certain patients with ceaseless AF.14

Parasympathetic incitement abbreviates the AERP and diminishes the frequency of atrial reentrant circuits.3 Besides shortening the AERP, vagal incitement builds the AERP scattering, which thus adds to the steadiness of AF.2151617 Although the specific job of the parasympathetic sensory system in incessant AF isn't clear at present, it appears to be sensible to estimate that a portion of the electrophysiological changes during ceaseless AF (ie, decline of the AERP and increment of the AERP scattering) might be in any event potentiated by the parasympathetic sensory system.

Possible Clinical Implications

Clinical ramifications of the proposed approach for transvascular atrial parasympathetic nerve framework alteration must be considered carefully until incessant creature examines confirm that no significant autonomic reinnervation or RPA stenosis will happen after the strategy. By the by, potential objective gatherings for such a methodology will be talked about quickly as point by point beneath.

Coumel and colleagues518 and later Chen et al6 have depicted subgroups of patients with paroxysmal AF with an increased parasympathetic tone. In these patients, antiarrhythmic specialists, for example, flecainide or amiodarone can effectively decrease the recurrence of AF eruptions. In certain patients who are impervious to amiodarone as well as flecainide, atrial pacing alone or notwithstanding antiarrhythmic drugs is extremely compelling in forestalling these arrhythmias. Atrial pacing reliably forestalls vagally prompted AF, accordingly indicating that it is in any event mostly bradycardia subordinate instead of vagally actuated. A few instances of this marvel are given by the intensive clinical investigations of Coumel and colleagues.518 The current examination proposes that for some AF patients with a raised vagal tone, transvenous parasympathetic nerve framework adjustment might be created as an elective treatment methodology. Curiously, this methodology additionally essentially blunted the sinus rate easing back during VNS. In spite of the fact that the result is theoretical, one could envision that in patients with vagal AF, the proposed removal methodology could dull both a vagally reliant sinus bradycardia and a vagally initiated shortening of the AERP. Be that as it may, the drawn out security and plausibility of the removal system must be exhibited in creatures before any suggestions for the treatment of patients with such a removal method are supported.

Indeed, even in AF patients with no conspicuous clinical proof of a raised parasympathetic tone, the prolongation of the benchmark AERP after intravascular atrial parasympathetic nerve framework change may have an antiarrhythmic impact. Albeit altogether along these lines, this benchmark AERP prolongation after removal was generally little in the current examination. In any case, it has must be considered that the pentobarbital sedation prompts a practically all out loss of the resting vagal tone.19 Thus, it is possible that the AERP prolongation after removal may in certainty be more noteworthy

with an alternate sort of sedation or without sedation.

Last, however not least, the Maze technique for the treatment of AF in part parasympathetically denervates the atria, as of late appeared by Elvan.20 Similarly, Chevalier et al21 showed that direct atrial myocardial injuries applied epicardially to the atria by means of thoracoscopy essentially diminished the inducibility of vagally actuated and looked after AF. Be that as it may, the refered to and different methodologies for the Maze strategy contrast essentially from the removal technique depicted in the current examination since they all apply direct atrial myocardial tissue sores. Paradoxically, in most of instances of the current investigation, sores were made in the incredible vessels outside the heart legitimate. In the event that a parasympathetic denervation adds to the achievement of the Maze methodology, the inquiry emerges regarding whether transvenous atrial parasympathetic nerve framework change as depicted in the current examination may lessen the necessary number of direct sores of a Maze strategy.

Study Limitations

Transvenous atrial parasympathetic nerve framework alteration likewise annulled the vagal prolongation of the sinus cycle length and AV conduction during two-sided VNS. Hypothetically, this could build the ventricular rate if AF ought to repeat after the removal method. We didn't test whether the thoughtful innervation of the sinus and AV hub was as yet protected after removal. In any case, past examinations have just demonstrated that careful analyzation of the parasympathetic nerves giving the atria and the AV and sinus hubs doesn't fundamentally influence the thoughtful innervation of these structures.1322 Therefore, a neural and humoral thoughtful regulation of the sinus rate and AV conduction may in any case be conceivable after removal. Actually, a slight increment of the sinus rate during reciprocal incitement of the vagosympathetic trunk after removal might be taken as a proof that the thoughtful innervation of the sinus hub is in any event mostly saved.

In the current examination, we didn't try to decide if the parasympathetic nerves at the RPA, IVC, and SVC locales likewise innervate the ventricles. In any case, we didn't watch a huge change in the ventricular unmanageable periods during RPA incitement in past studies.723 Similarly, different creators have recently demonstrated that epicardial pulverization of the parasympathetic fat cushions neighboring the RPA and IVC didn't influence the prolongation of the ventricular headstrong period that was because of respective VNS.24

In this intense creature model, removal in the RPA prompted circumscript noncircumferential injuries in the RPA. Naturally visible apoplexy at the removal locales was not watched despite the fact that the mutts were not anticoagulated. Notwithstanding, it is conceivable that removal in the RPA may cause pneumonic embolism or aspiratory stenosis in the long haul.

There might be worries with respect to whether the removal impact in the current investigation was because of a vague atrial removal impact as opposed to adjustment of the parasympathetic nerves. It ought to be accentuated that in 5 of the 7 canines, RFCA was confined to the RPA (n=4) or RPA and SVC (n=1). In these canines, removal was performed without an atrial passageway of the catheter. At the removal destinations in the RPA and in the SVC, electrical catch (pacing) of atrial myocardial tissue never happened or after RFCA. Or maybe, modified atrial incitement from the 7 atrial testing locales could be performed for AERP assurance during nerve incitement in the RPA and SVC. This is a solid proof that the removal impact at any rate in most of creatures was not because of an obliteration of atrial myocardial tissue. This is additionally upheld by the way that

perceptible investigation and histological assessments of the atria of the canines that were removed only in the RPA didn't uncover indications of atrial harm after the removal strategy.

In 1 creature, be that as it may, notwithstanding the RPA sores, a solitary RFCA sore (plainly visible length 4 mm, width 2 mm) was made at the back left sidelong quadrant of the IVC at its change to the correct chamber. In a subsequent canine, 2 sores (normal injury length 4 mm) were made at the back and left horizontal part of the IVC at its change to the correct chamber notwithstanding the RPA sores. In this manner, in these 2 canines, we can't reject that notwithstanding the removal sores outside the heart (in the RPA), an atrial myocardial removal impact may have added to the noninducibility of vagal AF. Significantly, the atrial sores in the IVC abrogated the shortening of the AERP during two-sided VNS at atrial locales far off from the removal site; this finding shows that a neural removal impact was likewise working. Also, from prior tests in which pharmacological nerve bar with atropine or hexamethonium lessened the negative dromotropic impact of high-recurrence incitement in the IVC,10 it is possible that parasympathetic nerves were invigorated at the IVC/right atrial site in these 2 dogs.

Conclusions

Parasympathetic nerves that innervate much of the atria may be stimulated and ablated in RPA, IVC, and SVC through the use of a transvenous catheter technique. Neural ablation destroys the vagal AF. Further testing of this anti-fibrillatory treatment in chronic AF animal models is necessary if a transvenous parasympathetic atrial alteration is to be clinically useful.

. Dorsal perspective on atria and incredible vessels is appeared. Course of nerves delineated is useful course as opposed to anatomically address portrayal of parasympathetic atrial innervation. The vast majority of right and left vagal filaments that innervate atria and sinus or AV hub meet to fat cushion between RPA, base of aorta, and SVC (RPA fat cushion [*]). Some vagal filaments that innervate atria are situated in fat cushion between IVC, left chamber, and ostium of coronary sinus (**) and along SVC. Incitement and removal of parasympathetic nerves was performed with expandable anode catheter, which was brought into upper RPA (n=7), SVC (n=1), or IVC (n=2).

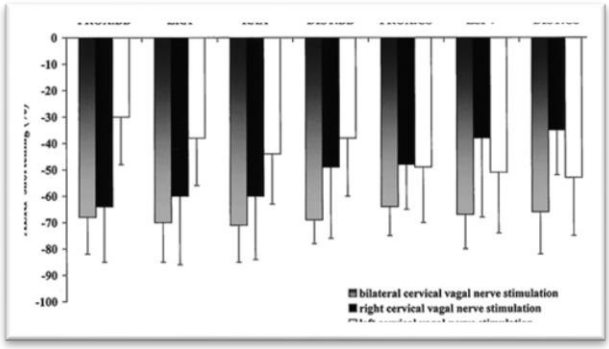

Figure 2. Percentage of AERP reduction at 7 atrial sites during unilateral / bilateral cervical VNS. PROX.BB and DIST.BB signify proximal and distal Bachmann bundle, respectively; PROX.CS and DIST.CS, proximal and distal coronary sinus, respectively; and LSPV, left upper pulmonary vein. Percent decrease of AERP during VNS relative to AERP without VNS is seen on absciss.

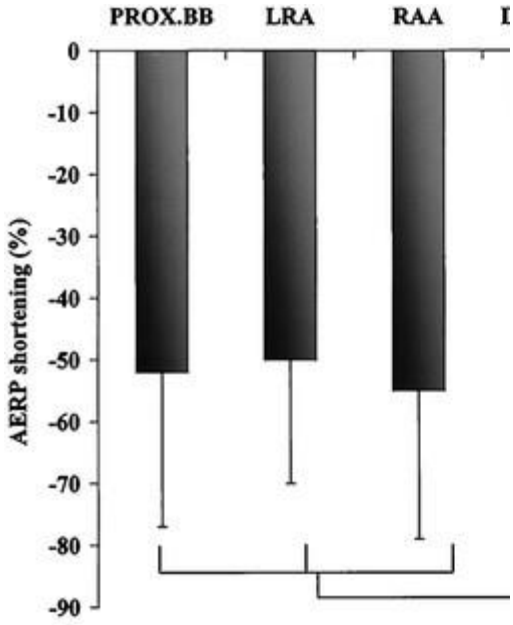

Figure 2. Impact of intravascular incitement of parasympathetic nerves in RPA on AERP. Percent lessening of AERP during vagal incitement contrasted and AERP without vagal incitement is portrayed on abscissa. RPA incitement essentially abbreviated AERP at all atrial locales contrasted and standard qualities (P<0.001 each). An essentially bigger diminishing of the AERP was seen at right atrial locales contrasted and left atrial destinations (P=0.02). Shortened forms as in Figure 2

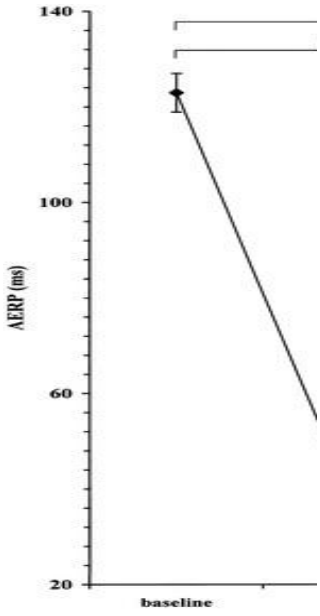

Figure 4. Effect of bilateral cervical VNS on AERP at all 7 atrial stimulation sites before and after RFCA. RFCA nearly eliminated AERP shortening during cervical VNS and contributed to a substantial improvement in baseline AERP after RFCA. * P<0.001 vs. baseline value.

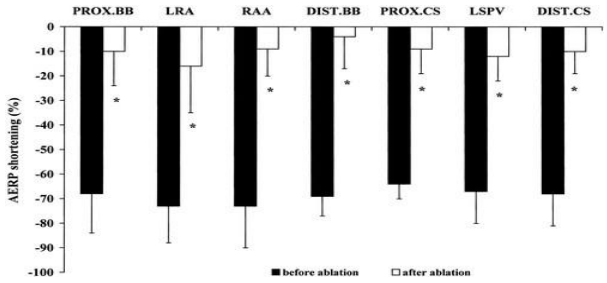

Figure 2. AERP shortening during the bilateral supramaximum cervical VNS before and after ablation. * P<0.001 vs. ablation. Abbreviations are shown in Figure 2.

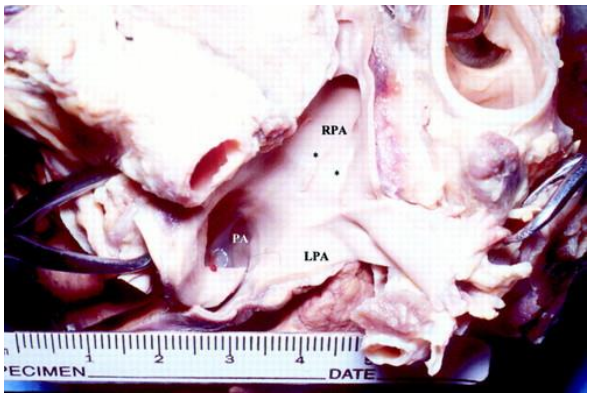

Figure 6. A macroscopic view of RPA following RFCA. Heart has been excised and set in formalin. The RPA has been sliced free. Short linear ablation lesions can be seen in the proximal RPA. LPA means left pulmonary artery; PA, pulmonary artery.

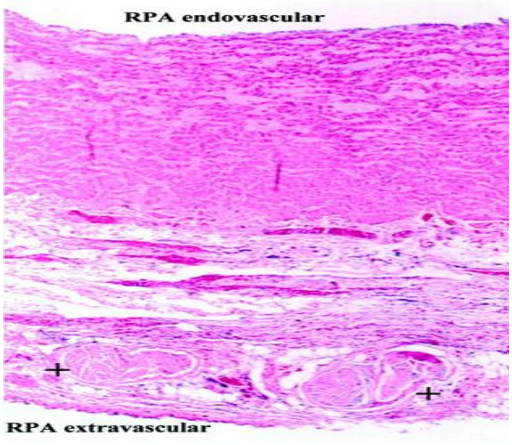

Figure 7. RPA histology. Various nerves (+) have been found in the fibrous and fatty tissues surrounding RPA.