Ablação da Fibrilação Atrial
Denervação Atrial

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O autor e seu grupo declaram não ter nenhum conflito de interesse.
Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2): A Randomized Trial

A Primary efficacy outcome

PV block entrance in 87% of cases

Cumulative Hazard Rate

Follow-up Since Randomization, d

No. at risk
Antiarrhythmic drug 61 61 35 25 21 18 17 17 12
Radiofrequency catheter ablation 66 66 46 39 32 30 28 27 18

HR, 0.56, 95% CI, 0.35-0.90, P = .02
Non-sustained Atrial Fibrillation Induced by Vagal Drive

Could the Denervation Improve the Ablation Outcomes?
Innervation Rule in AF

- Functional (Trigger Activity)
- Structural (Micro-reentry)
Innervation Rule in AF

• **Functional** *(Trigger Activity)*

• **Structural** *(Micro-reentry)*
Sinus Node Artery Acetylcholine and Adrenaline Infusion

Acetylcholine 1 uM/l

Adrenaline 10uM/l

B

10 uM Adrenaline + Atropine

HR=243bpm – No AF
ANS AF Induction - Ca$$^{++}$$ Transient

Achetylcholine

Early Post-Potential

Triggered Activity

Catecholamines

Ca$$^{++}$$ Transient

Patterson et al, Heart Rhythm, 06-2005
Innervation Rule in AF

• Functional (Trigger Activity)
• Structural (Micro-reentry)
Innervation Rule in AF

- Functional (Trigger Activity)
- Structural (Micro-reentry)
Validation of the Vagal Denervation

arrows are typical of tissues that present very short refractory period, out-of-phase conduction, reflection and micro-reen- named “Cardioneuroablation” and for investigating the phys- ionpathology of these arrhythmias.

[0050] FIG. 21 is an example of two spectra obtained by this method. On the left there is one spectrum of the compact myocardium. On the right one example of the “fibrillar myocardium” forming one “AF-Nest”. The “AF-Nests”, discov- ered by this method, are the real substratum of the atrial fibrillation and are also the regions of innervation entry in the atrial wall.

lar” myocardium (“AF nest”), B2 and B3. Therefore, time domain with high frequency filters may be used to map the “fibrillar” myocardium that must be ablated.

[0046] FIG. 17 shows on the left: a recording of the electrical activity of an “AF nest” in the left inter-atrial septum, pts.). There was no significant structural cardiopathy (EF=0. 63±0.4). The diagnoses were neurocardiogenic syncope 6 pts., intermittent high degree AV block 7pts. (3 of them occurring only while sleeping) and sinus dysfunction 13 pts. (being associated with brady-tachycardia syndrome in 9 pts.). All the patients were exhaustively studied by Holter, tilt-test, stress-
A Cardioneuro-Ablação promove uma significativa denervação parassimpática.

A modificação aguda da VRR-SDNN foi de 172 ± 57 para 109 ± 43 ms na fase crônica (p = 0.0009).
United States Patent
Pachon Mateos et al.

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

Jose C. Pachon M*, Enrique I. Pachon M, Juan C. Pachon M, Tasso J. Lobo, Maria Z. Pachon, Remy N.A. Vargas, Adib D. Jatene

The aim is to get significant long-lasting vagal response attenuation...
AF-Nests in Normal Heart

Atrial-Venous Junction

Muscle Bundles

PV
SVC
CS

Innervation Entrance

Loose and scattered myocardial cells in PV

Interpolation of neural fibers

Pachón

Europace. 2004 Nov;6(6):590-601
Background: Spectral analysis of the left atrium can identify high dominant frequency (DF) sites, which might play a role in the perpetuation of atrial fibrillation (AF). Furthermore, the role of the cardiac autonomic nervous system (CANS) in the genesis of AF has been demonstrated. The relationship between CANS and the high-DF sites (AF nest) was the aim of the investigation.

Methods and Results: In 12 dogs, high frequency stimulation was applied to locate 4 major left atrial (LA) ganglionated plexi (GPs). An Ensite Array and a mapping catheter were delivered into the left atrium for electroanatomical mapping. During sinus rhythm, spectral analysis was performed on the bipolar electrograms in the left atrium before and after epicardial GP ablation. The majority of AF nests were close to the GPs (52±18% of total AF nests). After GP ablation, the mean LA DF values decreased from 54±7 Hz to 49±4 Hz (P=0.023), and DF values of the AF nest decreased from 93±2 Hz to 87±4 Hz (P=0.001). Most of the previous AF nest sites close to the GPs disappeared (85±23%). The surface area of the AF nest decreased from 9±5 cm² to 3±2 cm² (P=0.001).

Conclusions: Catheter ablation of the GP decreased the DF values, AF nest areas and diminished the number of AF nests; particularly those close to the GPs, indicating that the CANS might play an important role in the mechanism of the AF nest. (Circ J 2014; 78: 922–928)

Key Words: Ablation; Atrial fibrillation; Autonomic; Ganglionated plexus
Conclusions: Catheter ablation of the GP decreased the DF values, AF nest areas and diminished the number of AF nests; particularly those close to the GPs, indicating that the CANS might play an important role in the mechanism of the AF nest. *(Circ J 2014; 78: 922–928)*
Fibrillar and Compact Myocardium Behaviour

**Fibrillar Myocardium** ↓ **Connexins**

- Trigger Activity
- Microreentry
- AF Induction

**Compact Myocardium** ↑ **Connexins**

- AF Induction
- Sinus Rhythm
Cardiac Mapping

Edited by
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Attending Physician
Department of Cardiovascular Services
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Advantage of multiple sites recording:
1. Degree of atrial remodeling
2. Locate the abnormal arrhythmogenic regions
3. Potential conduction isthmus

Electrogram

Spectral analysis

Advantage of single site time-domain signal
1. Voltage: identification of scar, slow conduction isthmus area.
2. Activation duration and deflection number: complexity of electrograms: related to substrate characteristics and possible parasympathetic innervation sites.

Frequency spectrum

Advantage of single site frequency-domain signal
High DF (AF nest sites): arrhythmogenic substrate and parasympathetic innervation sites (GP).
Denervation by AF-Nest Ablation

AF-Nest Pre-Ablation

AF-Nest Post-Ablation

RF

30-40J / 15-30s / 60°C
Anatomy of Ganglionated Plexi
Katritsis et al. HeartRhythm 2011 May;8(5):672-8
Validation of the Vagal Denervation

Simplified Method for Vagal Effect Evaluation in Cardiac Ablation and Electrophysiological Procedures

Jose C. Pachon M., MD, PhD,†† Enrique I. Pachon M., MD,*,†† Tomas G. Santillana P., MD,† Tasso J. Lobo, MD,† Carlos T.C. Pachon, MD,† Juan C. Pachon M., MD,*,†† Remy N. Albornoz V., MD,*,† Juan C. Zerpa A., MD†

ABSTRACT

OBJECTIVES The aim of this study is to show a simplified reversible approach to investigate and confirm vagal denervation at any time during the ablation procedure without autonomic residual effect.

BACKGROUND Parasympathetic denervation has been increasingly applied in ablation procedures such as in vagal-
How to Check the Vagal Denervation?
A very important step!
How to Check the Vagal Denervation?

- Right Vagal Stimulation
- Left Vagal Stimulation
- Right Internal Jugular Vein
- Left Internal Jugular Vein
Vagal Stimulation before CNA
A fundamental step!

Pause = 17.5 sec

Vagal Stimulation ON

Vagal Stimulation OFF
AF Induction by Vagal Stimulation
AF Induction by Vagal Stimulation

Pre AF-Nest Ablation

<table>
<thead>
<tr>
<th>Sinus Rhythm</th>
<th>Asytole</th>
<th>AF</th>
</tr>
</thead>
</table>

Vagal Stimulation

Post AF-Nest Ablation

<table>
<thead>
<tr>
<th>Sinus Rhythm</th>
</tr>
</thead>
</table>

Vagal Stimulation
Long-Lasting Persistent AF Ablation
Hcor Arrhythmia Service

Hybrid Approach

- Venous Isolation (PV, CS, SVC)........... Triggers Sbstratum

- AF-Nests Ablation.......................... Innervation Substratum

- Background Tachycardia Ablation... Driver
Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2): A Randomized Trial


A Primary efficacy outcome

AF Ablation Relapse Rate

Cumulative Hazard Rate

Follow-up Since Randomization, d

Antiarrhythmic drug

PVI

31%

PVI + GP ablation

60%

56%

PV block entrance in 87% of cases
PVI AF Ablation with and without GP Ablation
Meta-analysis of randomized controlled clinical trials

**a**

<table>
<thead>
<tr>
<th>All AF patients</th>
<th>PVI+GPA</th>
<th>PVI alone</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Driessen 2016</td>
<td>78</td>
<td>110</td>
<td>80</td>
</tr>
<tr>
<td>Katritsis 2011</td>
<td>25</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>Katritsis 2013</td>
<td>61</td>
<td>82</td>
<td>44</td>
</tr>
<tr>
<td>Pokushalov 2013</td>
<td>65</td>
<td>132</td>
<td>45</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>358</strong></td>
<td><strong>360</strong></td>
<td><strong>100.0%</strong></td>
</tr>
<tr>
<td>Total events</td>
<td>229</td>
<td>184</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.05; Chi² = 4.44, df = 3 (P = 0.22); I² = 32%
Test for overall effect: Z = 2.97 (P = 0.003)

**b**

<table>
<thead>
<tr>
<th>Paroxysmal AF</th>
<th>PVI+GPA</th>
<th>PVI alone</th>
<th>Odds Ratio</th>
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<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Driessen 2016</td>
<td>33</td>
<td>41</td>
<td>39</td>
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<tr>
<td>Katritsis 2011</td>
<td>25</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>Katritsis 2013</td>
<td>61</td>
<td>82</td>
<td>44</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>157</strong></td>
<td><strong>164</strong></td>
<td><strong>100.0%</strong></td>
</tr>
<tr>
<td>Total events</td>
<td>119</td>
<td>98</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 1.26, df = 2 (P = 0.53); I² = 0%
Test for overall effect: Z = 3.21 (P = 0.001)

**c**

<table>
<thead>
<tr>
<th>Persistent AF</th>
<th>PVI+GPA</th>
<th>PVI alone</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Driessen 2016</td>
<td>45</td>
<td>69</td>
<td>40</td>
</tr>
<tr>
<td>Pokushalov 2013</td>
<td>65</td>
<td>132</td>
<td>45</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>201</strong></td>
<td><strong>196</strong></td>
<td><strong>100.0%</strong></td>
</tr>
<tr>
<td>Total events</td>
<td>110</td>
<td>85</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.03; Chi² = 1.34, df = 1 (P = 0.25); I² = 26%
Test for overall effect: Z = 1.77 (P = 0.08)
PVI AF Ablation with and without Surgical GP Ablation

The AF ACT Study

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>All</td>
<td>240</td>
<td>1.01 [0.74-1.39]</td>
<td>0.93</td>
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<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 yr</td>
<td>126</td>
<td>1.02 [0.67-1.55]</td>
<td>0.94</td>
</tr>
<tr>
<td>&gt;60 yr</td>
<td>114</td>
<td>1.02 [0.62-1.62]</td>
<td>1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>175</td>
<td>1.02 [0.71-1.46]</td>
<td>0.93</td>
</tr>
<tr>
<td>Female</td>
<td>65</td>
<td>1.01 [0.54-1.89]</td>
<td>0.98</td>
</tr>
<tr>
<td>AF Type</td>
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<td></td>
<td></td>
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<tr>
<td>Paroxysmal AF</td>
<td>98</td>
<td>0.98 [0.61-1.55]</td>
<td>0.92</td>
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<tr>
<td>Persistent AF</td>
<td>141</td>
<td>1.04 [0.68-1.61]</td>
<td>0.84</td>
</tr>
<tr>
<td>LA Volume Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;33 ml/m²</td>
<td>72</td>
<td>1.08 [0.64-1.83]</td>
<td>0.78</td>
</tr>
<tr>
<td>33-40 ml/m²</td>
<td>60</td>
<td>1.05 [0.54-1.85]</td>
<td>1</td>
</tr>
<tr>
<td>&gt;40 ml/m²</td>
<td>103</td>
<td>0.97 [0.58-1.62]</td>
<td>0.88</td>
</tr>
<tr>
<td>AF duration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>146</td>
<td>1.04 [0.69-1.56]</td>
<td>0.84</td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>94</td>
<td>0.97 [0.59-1.61]</td>
<td>0.91</td>
</tr>
<tr>
<td>CHA²DS₂-VASc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>67</td>
<td>1.04 [0.66-1.81]</td>
<td>0.9</td>
</tr>
<tr>
<td>1</td>
<td>76</td>
<td>1.05 [0.58-1.89]</td>
<td>0.88</td>
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<tr>
<td>2</td>
<td>60</td>
<td>1.05 [0.54-1.86]</td>
<td>1</td>
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<tr>
<td>&gt;2</td>
<td>37</td>
<td>0.93 [0.42-2.17]</td>
<td>0.86</td>
</tr>
<tr>
<td>History of PVI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>56</td>
<td>1.01 [0.51-1.99]</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>183</td>
<td>0.97 [0.47-1.69]</td>
<td>0.94</td>
</tr>
</tbody>
</table>
Conclusion
Does Vagal Denervation must be done in AF Ablation?

• Yes, whenever possible!

• Vagal denervation makes the AF induction less probable

• Recent Meta-analysis has showing better results adding Vagal Denervation to PVI in PAF

• GP ablation and/or AF-Nest ablation may contribute to improve the AF catheter ablation results.
Thank You!

Aerial Photography: DR. LUIZ ÂNGELO PEIXOTO