CARDIONEUROABLATION FOR VASOVAGAL SYNCOPE

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Disclosure Slide

No disclosures

Vasovagal Syncope

- Vasovagal syncope (VVS) is the most common cause of transient loss of consciousness

- VVS:
  - may occur with upright posture (standing or seated or with exposure to emotional stress, pain, or medical settings;
  - typically characterized by diaphoresis, warmth, nausea, and pallor;
  - associated with vasodepressor hypotension and/or inappropriate bradycardia
  - often preceded by identifiable triggers and/or by a characteristic prodrome and often followed by fatigue

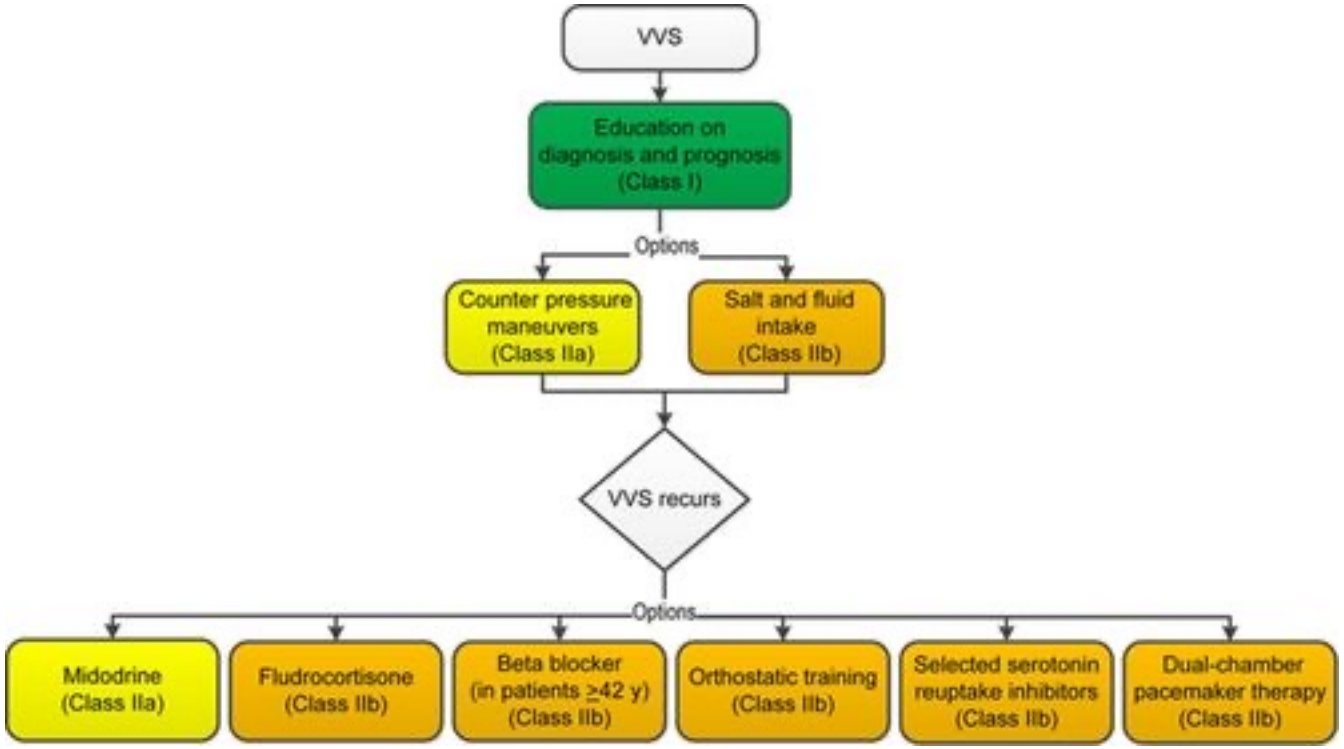
ACC/HRS Guidelines 2017

VASOVAGAL SYNCOPE INTERNATIONAL STUDY CLASSIFICATION

Type 1 mixed	Heart rate falls at the time of syncope, but the ventricular rate does not fall to less than 40 bpm or falls to less than 40 bpm for less than 10 s with or without asystole of less than 3 s. Blood pressure falls before the heart rate falls
Type 2A, cardioinhibition without asystole	Heart rate falls to a ventricular rate less than 40 bpm for more than 10 s, but asystole of more than 3 s does not occur. Blood pressure falls before the heart rate falls
Type 2B, cardioinhibition with asystole	Asystole occurs for more than 3 s. Heart rate fall coincides with or precedes blood pressure fall
Type 3 vasodepressor	Heart rate does not fall more than 10%, from its peak, at the time of syncope
Exception 1, chronotropic incompetence	No heart rate rise during the tilt (i.e., less 10% from the pre-tilt rate)
Exception 2, excessive heart rate rise	Excessive heart rate rise both at the onset of the upright position and throughout its duration before syncope (i.e., greater than 130 bpm)

M. Brignole et al *EP Europace*, January 2000,

Management of Vasovagal Syncope



Win-Kuang Shen. Circulation. 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society, Volume: 136, Issue: 5, Pages: e60-e122, DOI: (10.1161/CIR.0000000000000499)

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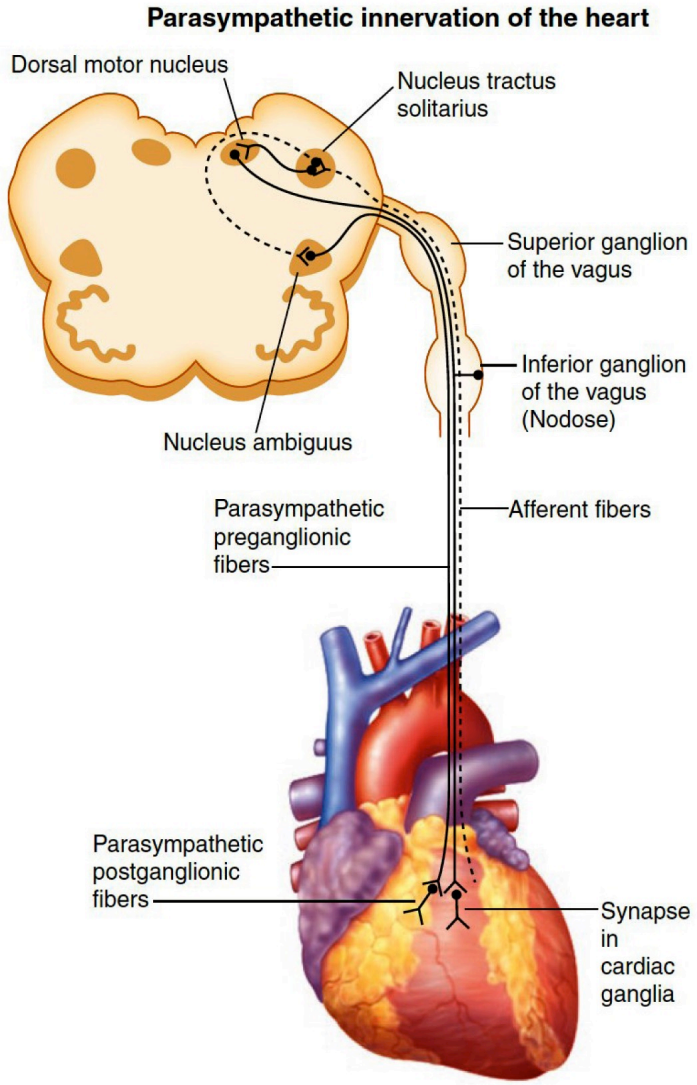
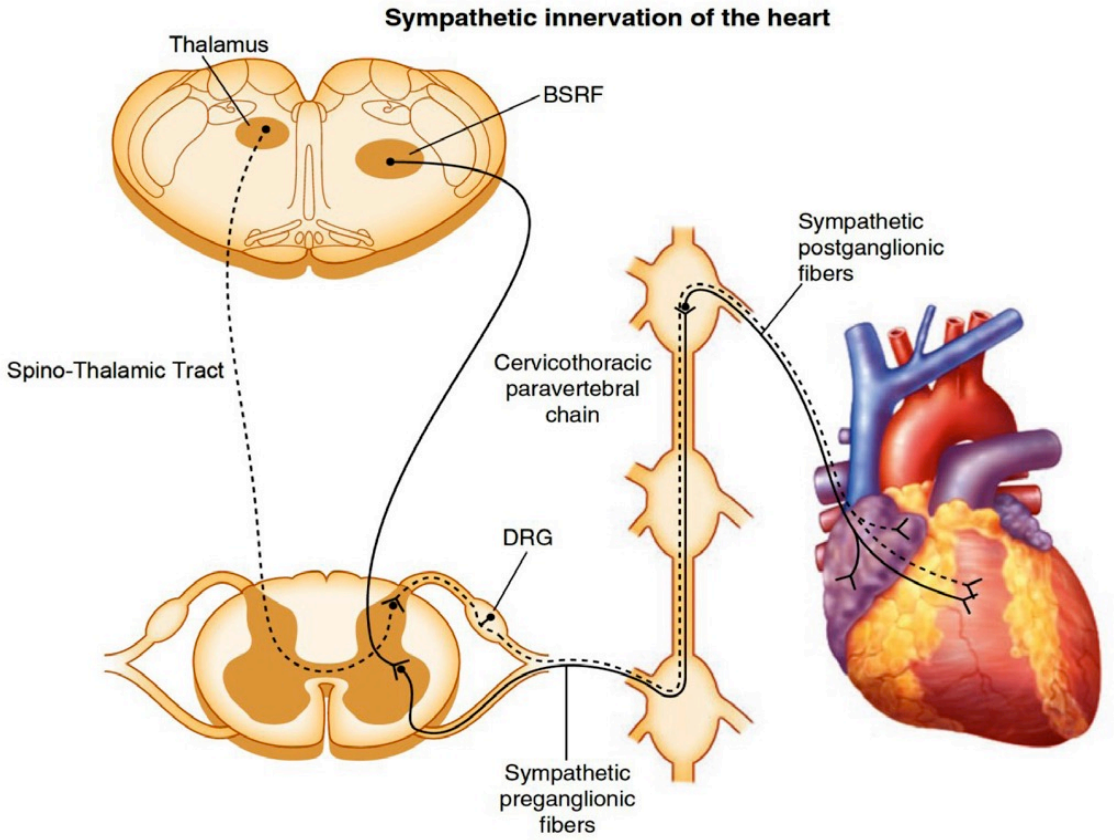




Parasympathetic ganglia are located around the epicardial fat pads in discrete locations – referred to as ganglionic plexi or GPs

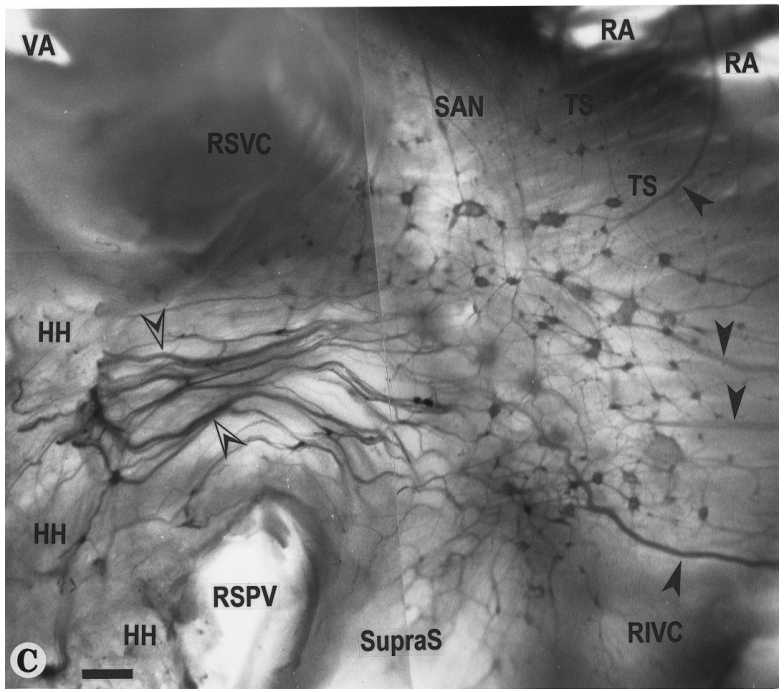
Sympathetic ganglia are located in the paravertebral chain thus away from the cardiac structures.

Human Epicardial Ganglionic Plexi

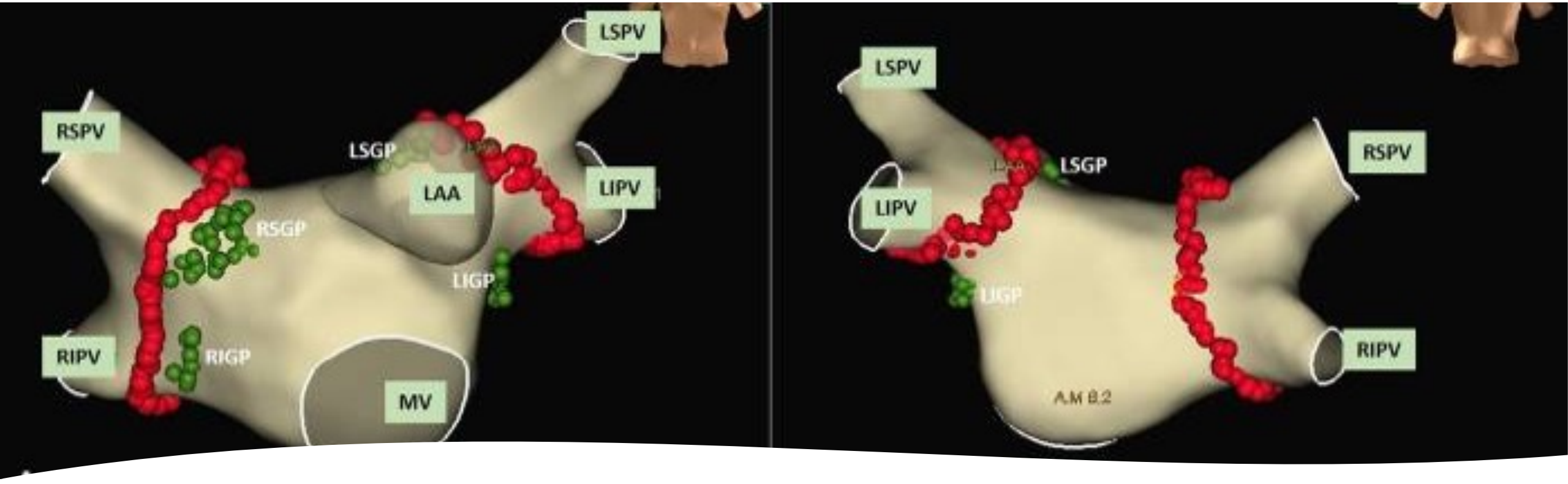
- More ganglia are across the epicardial surface of the heart – denser near the sinoatrial and atrioventricular region

- Fibres from these ganglionic cells penetrate the epicardium to reach the endocardium

- GP neurons classified as
- **1) afferent neurons from the atrial myocardium and central autonomic nervous system;**
- **2) efferent neurons from cholinergic and adrenergic neurons; and**
- **3) interconnecting neurons, which allow communication amongst afferent and efferent neurons**



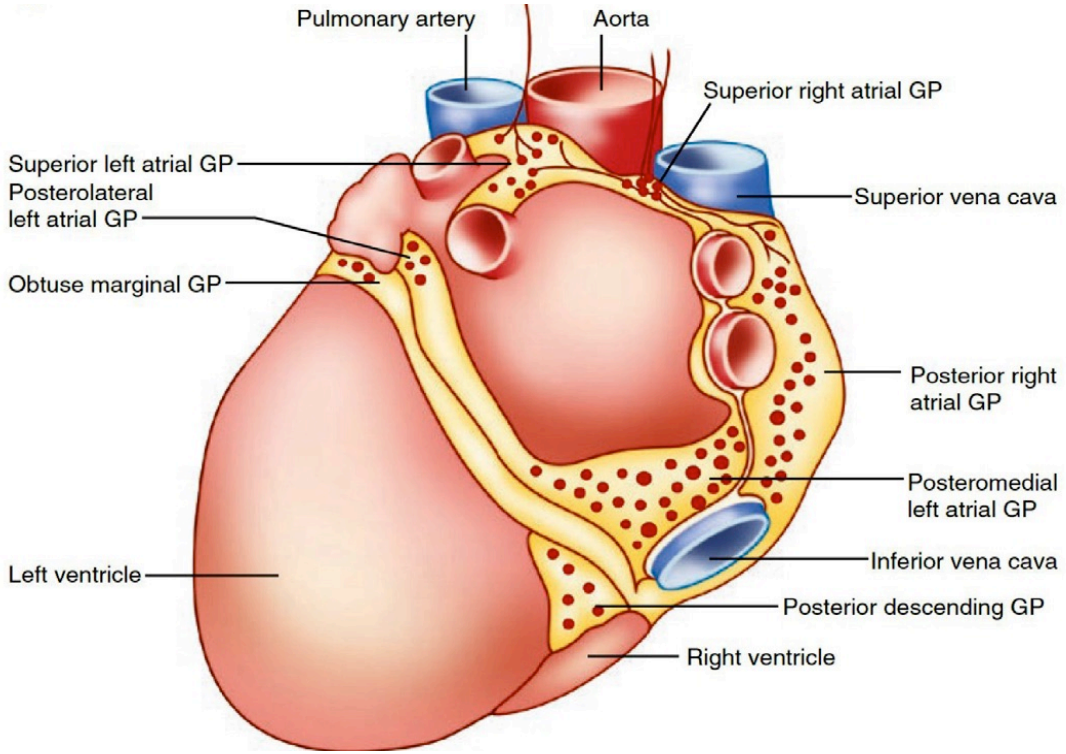
Pauza et al Anat. Rec., 259: 353-382.

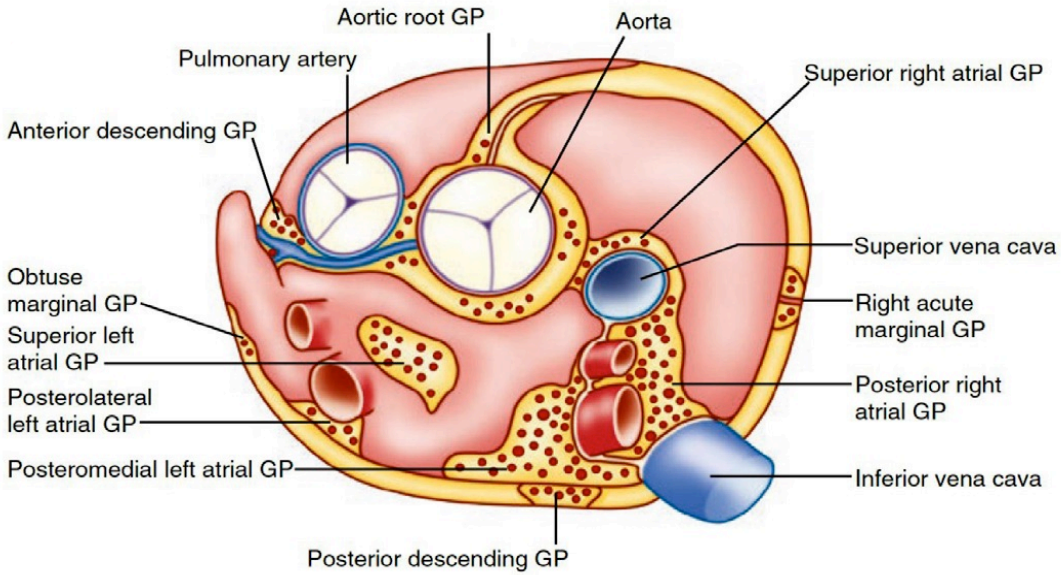


GP Ablation in Atrial Fibrillation

- Radiofrequency ablation of the ganglionic plexus or the efferent neurons has been thought to prevent atrial fibrillation during ablation.
- Animal studies have shown that ablation of parasympathetic ganglia does not influence sympathetic ganglia mediated effects as the epicardial region contains fibres while the ganglia are away from the cardiac structures.

Hardy C et al : Role of Ganglionated Plexus Ablation in Atrial Fibrillation on the Basis of Supporting Evidence. J Atr Fibrillation. 2020 Jun 30;13(1):2405.

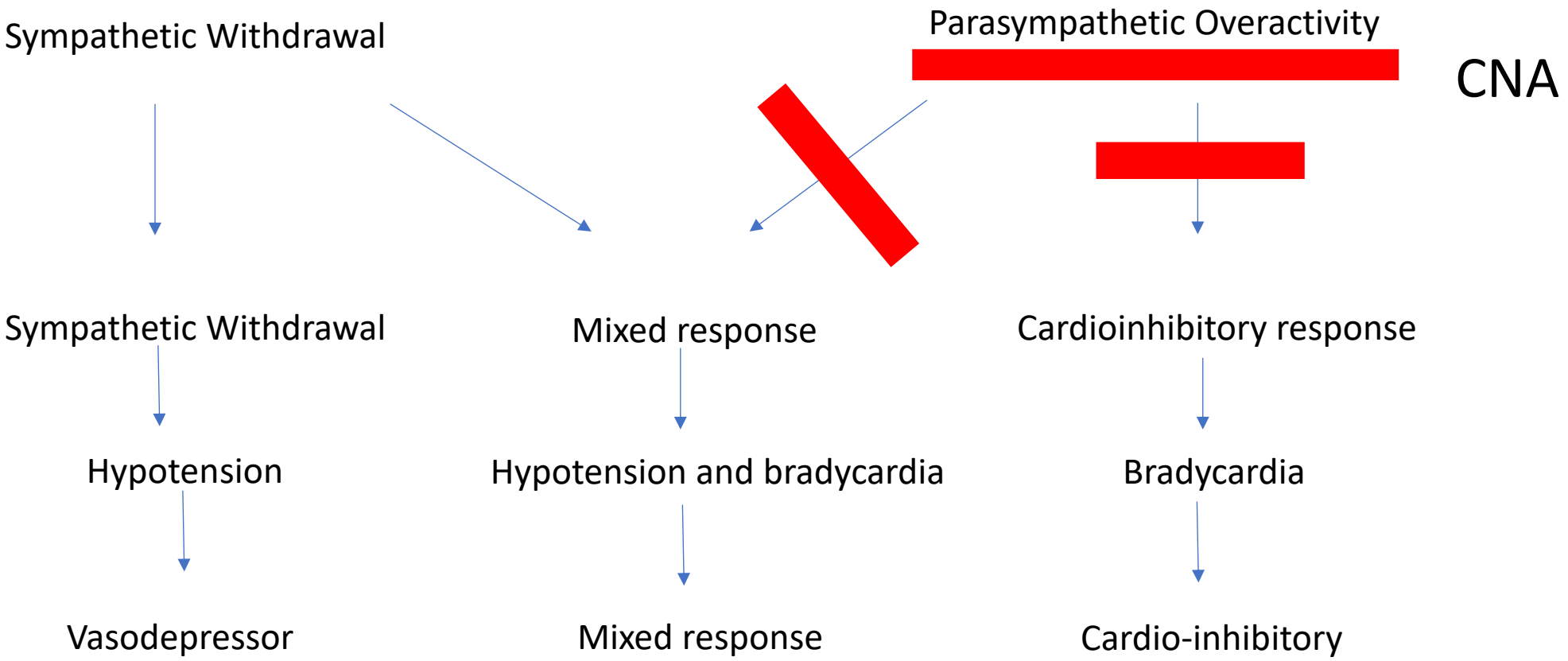




- Majority of papers agree with 7 regions with concentration of GPs
- 4 regions in the left atrium – left superior GP (LSGP) –the left inferior GP (LIGP) –the right inferior GP (RIGP) –the right anterior GP (RAGP).
- Others – Marshall tract GP (MTGP), located along the Coumadin ridge; infero-posterior fractionated atrial potentials posterior left atrial wall and between the left and right PV and coronary sinus

Armour J A. Gross and microscopic anatomy of the human intrinsic cardiac nervous system. Anat. Rec. 1997 Feb;247 (2):289–98

Likely Mechanism for varying HUTT responses in VVS

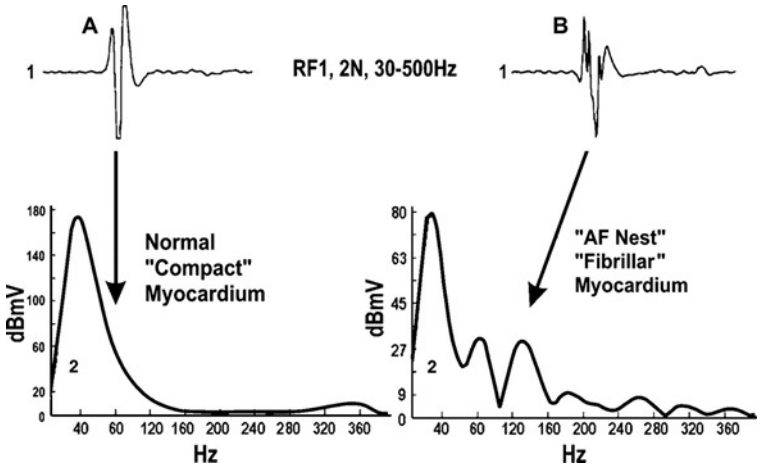


TECHNIQUE OF CARDIONEUROABLATION FOR VASOVAGAL SYNCOPE

- Selection of target areas
- Identification of ganglionic plexi
- Ablation – defining strategy and endpoints
- Post ablation followup

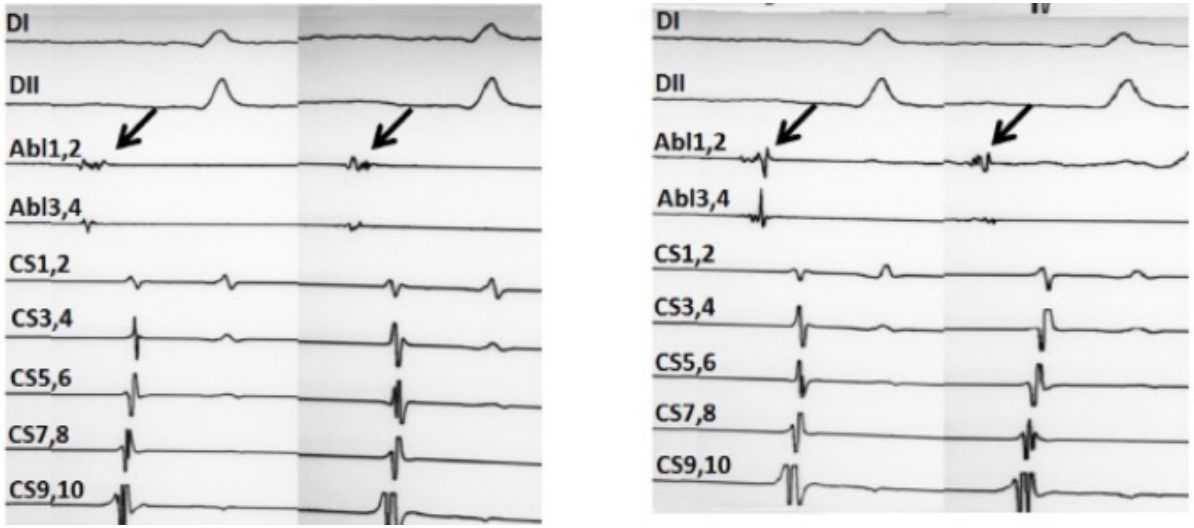
TECHNIQUE OF CARDIONEUROABLATION FOR VASOVAGAL SYNCOPE
Selection of target Areas

Spectral guided method



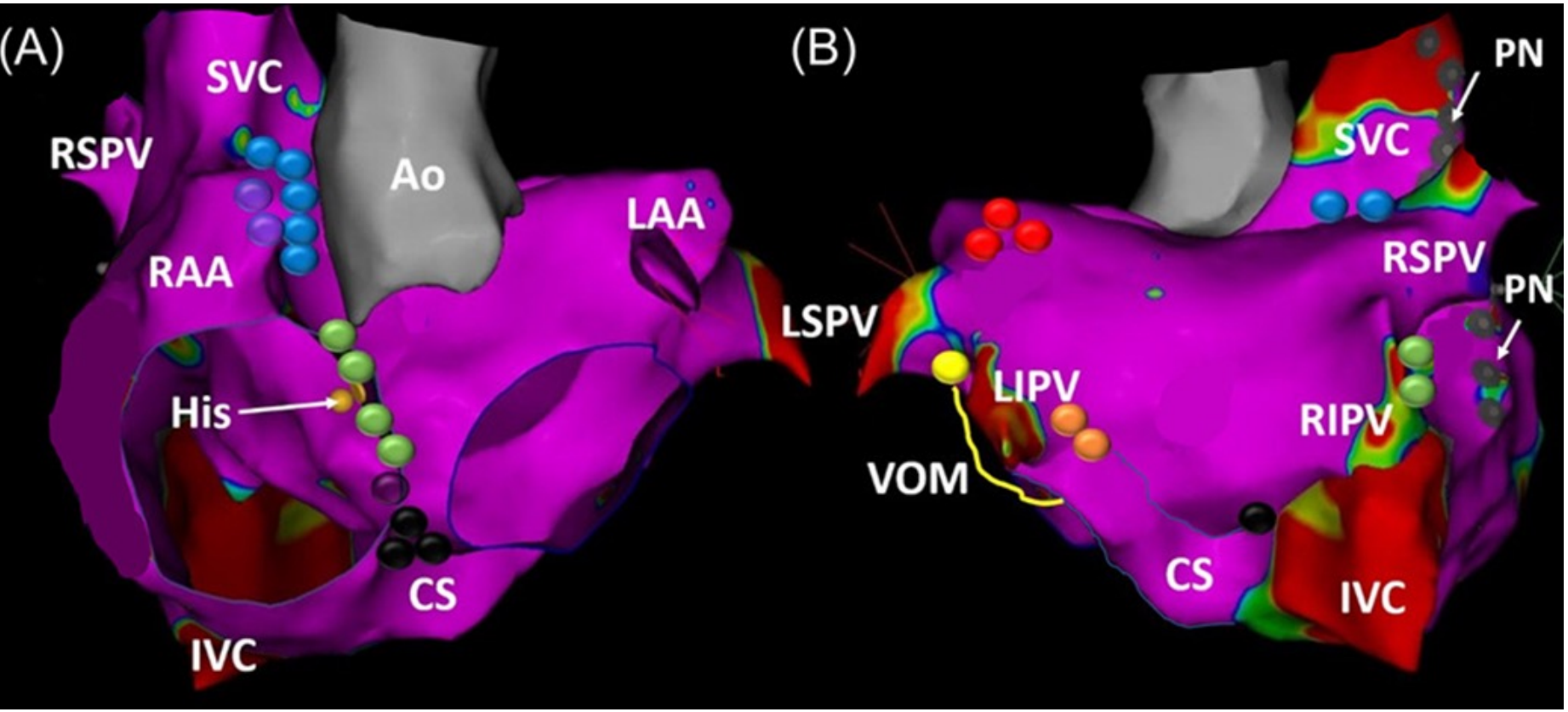
Used by Pachon et al (2005) to identify " fibrillar myocardium " and thus areas of "AF nests" in their 2004 study.
Limited by lack of availability of the technology

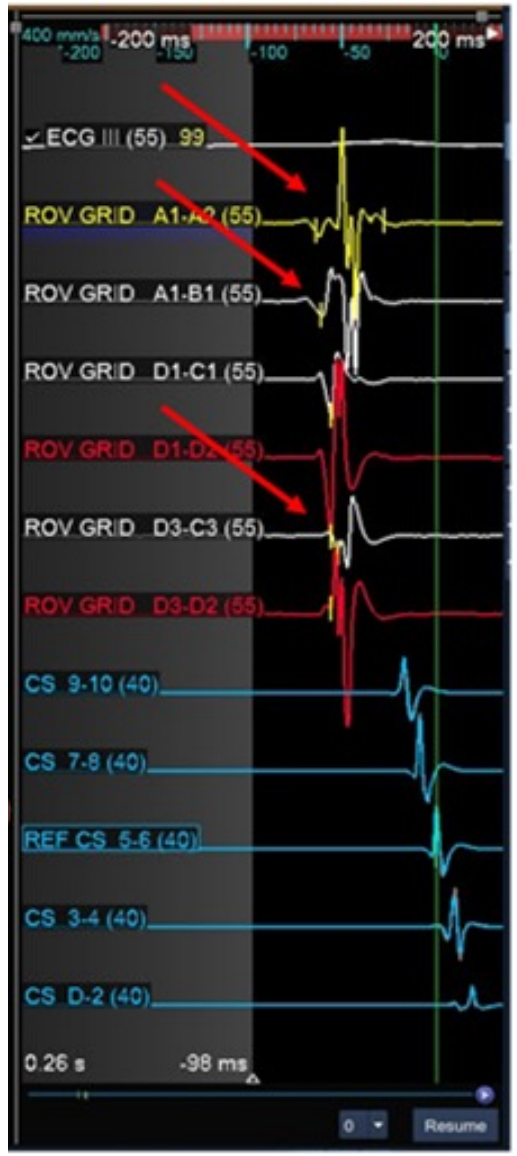
3 D Electroanatomical mapping



Most common method. Aksu et al (2015) used high and low Atrial fractionated potentials during 3-Dimensional mapping to identify atrial endocardial sites that showed proximity to GPs

TECHNIQUE OF CARDIONEUROABLATION FOR VASOVAGAL SYNCOPE
3-Dimensional Mapping



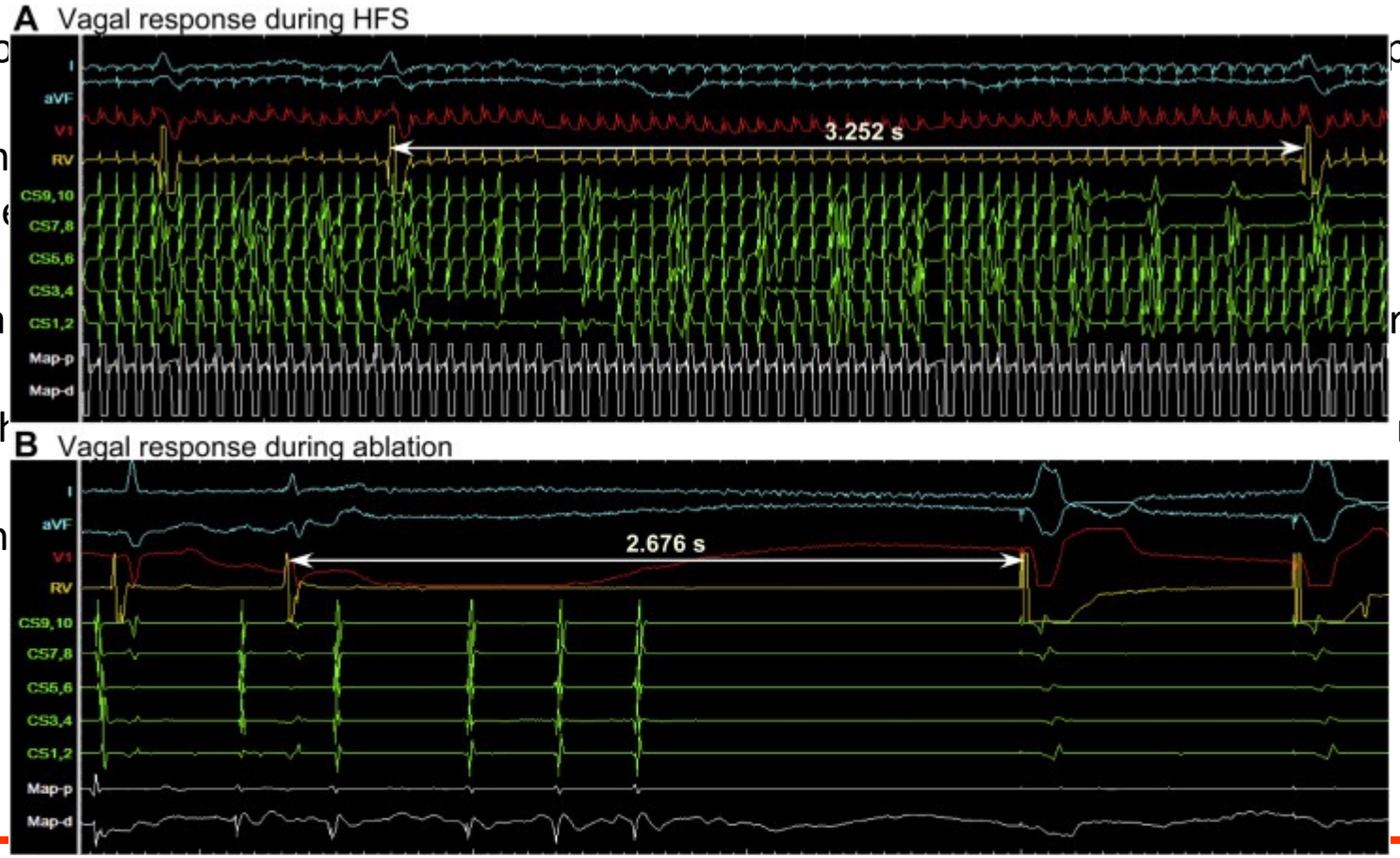


Aksu, T, Gupta, D, D'Avila, A, Morillo, CA. Cardioneuroablation for vasovagal syncope and atrioventricular block: a step-by-step guide. J Cardiovasc Electrophysiol. 2022; 1- 8

TECHNIQUE OF CARDIONEUROABLATION FOR VASOVAGAL SYNCOPE

Identification of ganglionic plexi or GPs and ablation

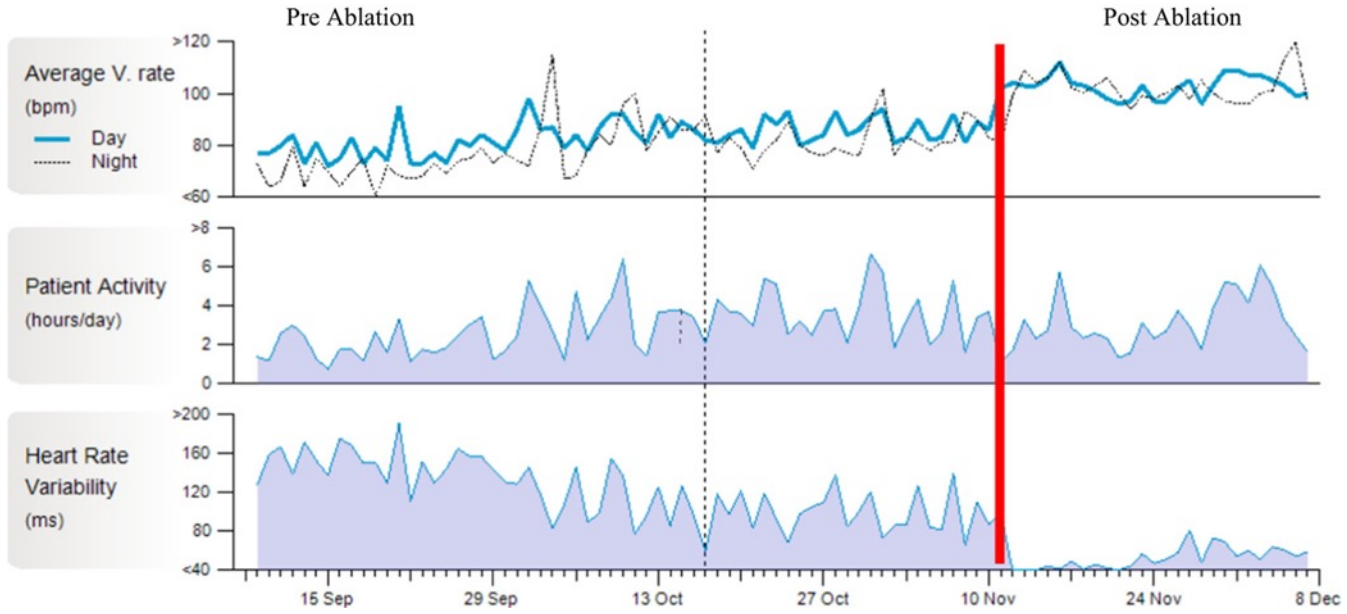
- Most commo potentials
- High frequen duration of 5 ms is delivered to
- Positive vaga rval increased by 50%
- Ablation at th marker.
- Post ablation



TECHNIQUE OF CARDIONEUROABLATION FOR VASOVAGAL SYNCOPE

Atropine response serves as ablation endpoint during the study

Most patients are then closely followed up. ILR implantation can help with remote followup.



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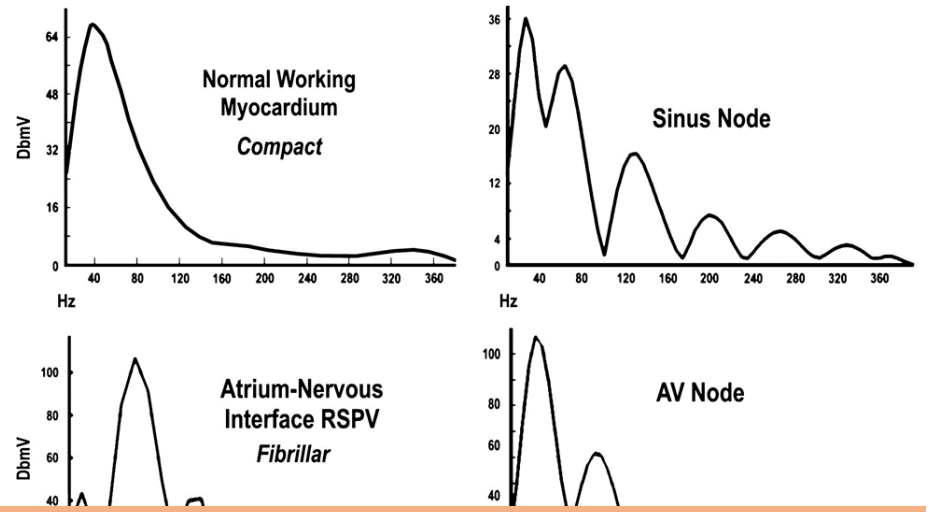
Cardiovasc electrophysiol, 2021Volume: 32, Issue: 6, Pages: 1748-1753,

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

- 21 patients with mean age 47.5 ± 16 range 19–70 years, presenting symptomatic functional bradyarrhythmias despite conventional therapy
- 6 patients had reflex mediated syncope. Rest had sinus node dysfunction and high-grade AV block.
- Ablations in both left and right atria.
- All the patients having neurally mediated reflex syncope were studied again with tilt-test 1 and 6 months after the ablation. Repeat Holter 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.



Heart rate variability decreased from 183±42 ms to 99±36ms (P<0.005)

All patients reported no syncope at the end of follow-up with 4/5 having negative tilt table studies – with one having vasodepressor response

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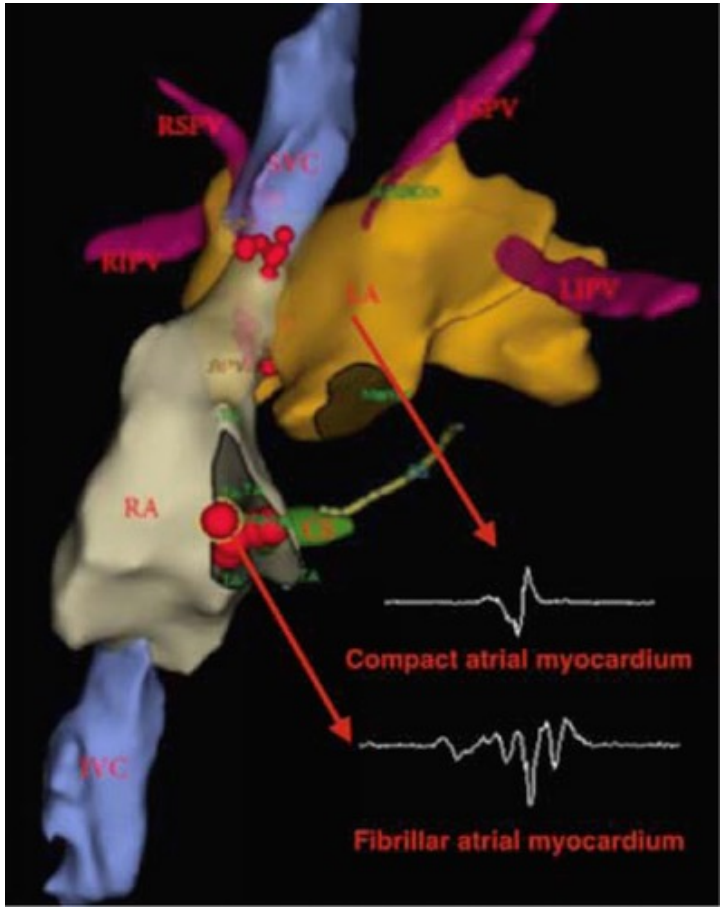
Jose C. Pachon M, *EP Europace*, Volume 7, Issue 1, 2005, Pages 1–13

Simplified Cardioneuroablation in the Treatment of Reflex Syncope, Functional AV Block, and Sinus Node Dysfunction

- 22 patients presenting symptomatic functional bradyarrhythmias, neurally mediated reflex syncope (NMS), symptomatic atrioventricular (AV) block, and symptomatic sinus node dysfunction (SND; number = 8, 7, 7)
- The three main paracardiac ganglia were targeted via RA and LA in the patients with NMS and SND.
- Fragmented potentials were identified by electrical mapping and verified by high-frequency stimulation and ablated until atrial electrical potential was completely eliminated (<0.1 mV).



Results

The patients with NMS and SND were free from new syncopal episode at a mean 12.3 ± 3.4 months and 9.5 ± 3.1 months follow-up. 6/7 patients with AV Block had no syncope at the end of followup.

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T.Aksu et al, Pacing and Clinical Electrophysiology, 39: 42-53

Right anterior ganglionated plexus: The primary target of cardioneuroablation?

Feng Hu, MD, Lihui Zheng, MD, PhD, Erpeng Liang, MD, Ligang Ding, MD, PhD, Lingmin Wu, MD, Gang Chen, MD, Xiaohan Fan, MD, PhD, Yan Yao, MD, PhD, FHRS

- 115 consecutive patients with VVS with ≥ 3 syncopal episodes were enrolled.
- GPs of the LA were identified by high-frequency stimulation and/or anatomic landmarks being targeted by radiofrequency catheter ablation.

- During ablation of right anterior ganglionated plexus (RAGP), heart rate increased from 61.3 ± 12.2 bpm to 82.4 ± 14.7 bpm (P < .001), whereas during ablation of other GPs only vagal responses were observed.

- During follow-up of 21.4 ± 13.1 months (median 18 months), 106 participants (92.2%) had no recurrence of syncope or presyncope.

- Holter data showed that m … time points (all P< .05), and mean heart rate rema … = .001).

Majority of patients (74.8 %) had a mixed HUTT response. However even patients with pure vasodepressor response benefitted from CNA

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Hu F. Heart Rhythm. 2019 Oct;16(10):1545-1551.

Cardioneuroablation for reflex syncope: efficacy and effects on autonomic cardiac regulation- A Prospective Randomized Trial

- First prospective, open, randomized, controlled, investigator-initiated trial comparing CNA vs optimal non-pharmacological therapy in patients with cardioinhibitory VVS.
- Inclusion- documented symptomatic cardioinhibitory or mixed VVS and positive atropine test.
- CNA was performed using RF ablation of the ganglionated plexi from the left and right atrium.
- Follow-up lasted 2 years. Primary endpoint was time to first syncope recurrence.
- Secondary endpoints included changes in sinus rhythm (SR) and heart rate variability (HRV) measured in Holter ECG at baseline and 3, 12 and 24 months after CNA as well as changes in quality of life (QoL) at baseline and after completion of follow-up.

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Piotrowski MD R, Baran J, Sikorska A, et al. Cardioneuroablation for reflex syncope: efficacy and effects on autonomic cardiac regulation- A Prospective Randomized Trial. J Am Coll Cardiol EP. null2022, 0 (0) .

Cardioneuroablation for reflex syncope: efficacy and effects on autonomic cardiac regulation- A Prospective Randomized Trial

Results

- 48 patients (17 males, mean age 38±10, 24-CNA group, 24-control group) entered the study.
- The primary endpoint occurred in 2 (8%) patients from the CNA group vs. 13 (54%) controls (p=0.0004).
- QoL significantly improved in the CNA group (30±10 vs 10±7 points, p=0.0001) whereas remained stable in controls (31±10 vs 30±10 points, p=0.5501

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Piotrowski MD R, Baran J, Sikorska A, et al. Cardioneuroablation for reflex syncope: efficacy and effects on autonomic cardiac regulation- A Prospective Randomized Trial. J Am Coll Cardiol EP. null2022, 0 (0) .

LIMITATIONS AND CONCERNS

- Continues to be investigational with most studies being single center studies. One small RCT till date with only 48 patients. Most recent meta-analysis had about 465 patients.
- Different methods by different operators – variation in ablation technique. Site of ablation , type of catheters
- Questionable benefit in patients with a pure Type 2 or Vasodepressor response. HUTT responses may vary in the same person
- High frequency stimulation may induce atrial fibrillation
- Most studies have followed up patients for upto 1 year in published data. Longer follow-up needed.
- Durability , patients with comorbidities, reflex tachycardia, age group, cost

SUMMARY

- CNA is a feasible and valuable adjunctive therapy in patients with VVS, vagal induced atrioventricular block and sinus node dysfunction.

- May have the ability to influence guidelines especially in a small subset – Cardioinhibitory response during HUTT in patients less than 40 years old where there is no good treatment. For patients more than 40 years pacemaker placement is currently a class II b recommendation (ACC 2017 Guidelines).

- Multicenter randomized-controlled trials may be required with possible comparison with a sham control or pacemaker placement given the placebo response to treatment in some patients.

THANK YOU

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