

Cardioneuroablation for reflex syncope - interim analysis of a randomized trial

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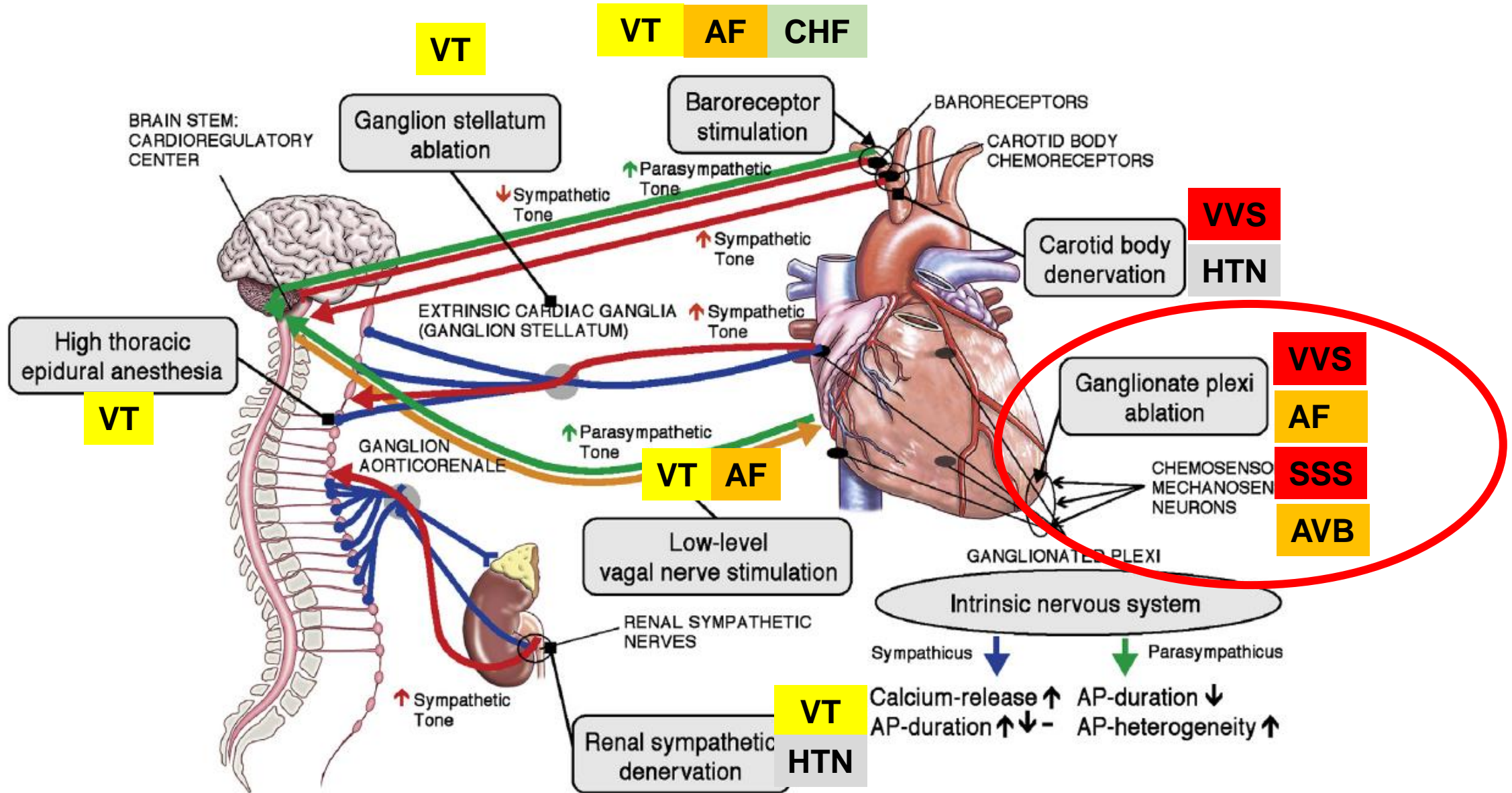
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Conflict of interest: none

Neuromodulation - possibilities



Vasovagal syncope (VVS) - some facts

- VVS - the most common cause of a transient loss of consciousness
- Patients with VVS – poor quality of life and high risk of syncope-related physical injury
- Parasympathetic hyperactivity – mechanism causing bradycardia and/or asystole and syncope
- Typical treatment for VVS – often ineffective
- Pacemaker implantation should be avoided
- Cardioneuroablation (CNA) may eliminate hyperactivity vagal tone and prevent asystole and syncope

Data confirming the effectiveness of CNA is still growing...

Author, year	VVS cases (n)	Method of CNA	Ablated GP	CNA approach	Syncope recurrence (%)	Mean follow up (months)
Pachon et al. <i>Europace</i> 2015	VVS = 5, AVB = 7 SND = 13	SM + AA	RAGP, RIGP, LIGP	BiA	0	9
Pachon, et al. <i>Europace</i> 2011	VVS = 43	SM + AA	RAGP, RIGP, LIGP	BiA	7	45
Pachon, et al. <i>CAE</i> 2020	VVS=80	SM + AA	RAGP, RIGP, LIGP	BiA	20	40
Yao et al. <i>Circ AE.</i> 2012	VVS = 10	HFS	RAGP, LSGP, LIGP	LA	0	30
Rebecchi et al. <i>JICE</i> 2012	VVS = 2	AA	RAGP, RIGP, LIGP,	RA	0	6.5
Aksu et al. <i>PACE</i> 2016	VVS = 8, AVB = 7 SND = 7	SM+AA+HFS	RAGP, RIGP, LIGP	BiA	0	11
Sun et al. <i>JAHA</i> 2016	VVS = 57	HFS (n = 10), AA (n = 37)	RAGP, RIGP, LSGP, LIGP LLGP	LA	0 (HFS) 13 (AA)	36
Rivarola et al. <i>Circ AE</i> 2017	VVS = 5, AVB = 10	AA	RAGP, RIGP, LSGP, LIGP	BiA	0 (VVS) 40 (AVB)	22
Debruyne et al. <i>Circ AE</i> 2018	VVS = 20	AA	RAGP	RA	25	6
Piotrowski et al. <i>Kardiol Pol</i> 2018	VVS = 3	AA	RAGP, RIGP	BiA	0	13
Hu et al. <i>Heart Rhythm.</i> 2019	VVS = 123	AA + HFS	RAGP, RIGP, LSGP, LIGP	LA	4	21
Aksu et al. <i>JICE</i> 2020	VVS = 46, AVB = 11 SND= 8 BiA = 58, RA = 7	AA + HFS (Group 1) SM+AA+HFS (Group 2)	BiA: RAGP, RIGP, LSGP, LIGP RA: RAGP, LIGP	BiA RA	0 (VVS) 27 (AVB) 0 SND	VVS = 15 AVB = 35 SND = 25
Aksu et al. <i>Europace</i> 2020	VVS = 51	AA + HFS + AA	BiA: RAGP, RIGP, LSGP, LIGP RA: RAGP, LIGP	BiA	6	11
May et al. <i>Indian Pace</i> 2020	VVS = 26	AA (CB)	RAGP, RIGP, LSGP	LA	16	20
Lu et al. <i>Chin Med. J.</i> 2020	VVS = 13	SM + AA	RAGP, RIGP	RA	16	13
Aksu et al. <i>JICE</i> 2021	VVS=51, control=50	AA	?	?	6 (VVS) vs 18 (control)	20
Calo et al. <i>JICE</i> 2020	VVS = 18	AA	RAGP, RIGP	RA	16	34
Total	N = 624				10 (0-40)	21 (5-45)

What the guidelines say?

**2017
ACC/AHA/HRS**



„Preliminary data from cardiac ganglia plexi ablation in treating selected patients with VVS are encouraging but still insufficient to make recommendations at this time”

2018 ESC



„Radiofrequency ablation of vagal ganglia located close to the sinus node and AV node was reported to abolish the vagal efferent output during VVS in some observational studies and case reports. However, owing to a weak rationale, small populations, weak documentation of follow-up results, procedural risks, and lack of control groups, the current evidence is insufficient to confirm the efficacy of vagal ganglia ablation”

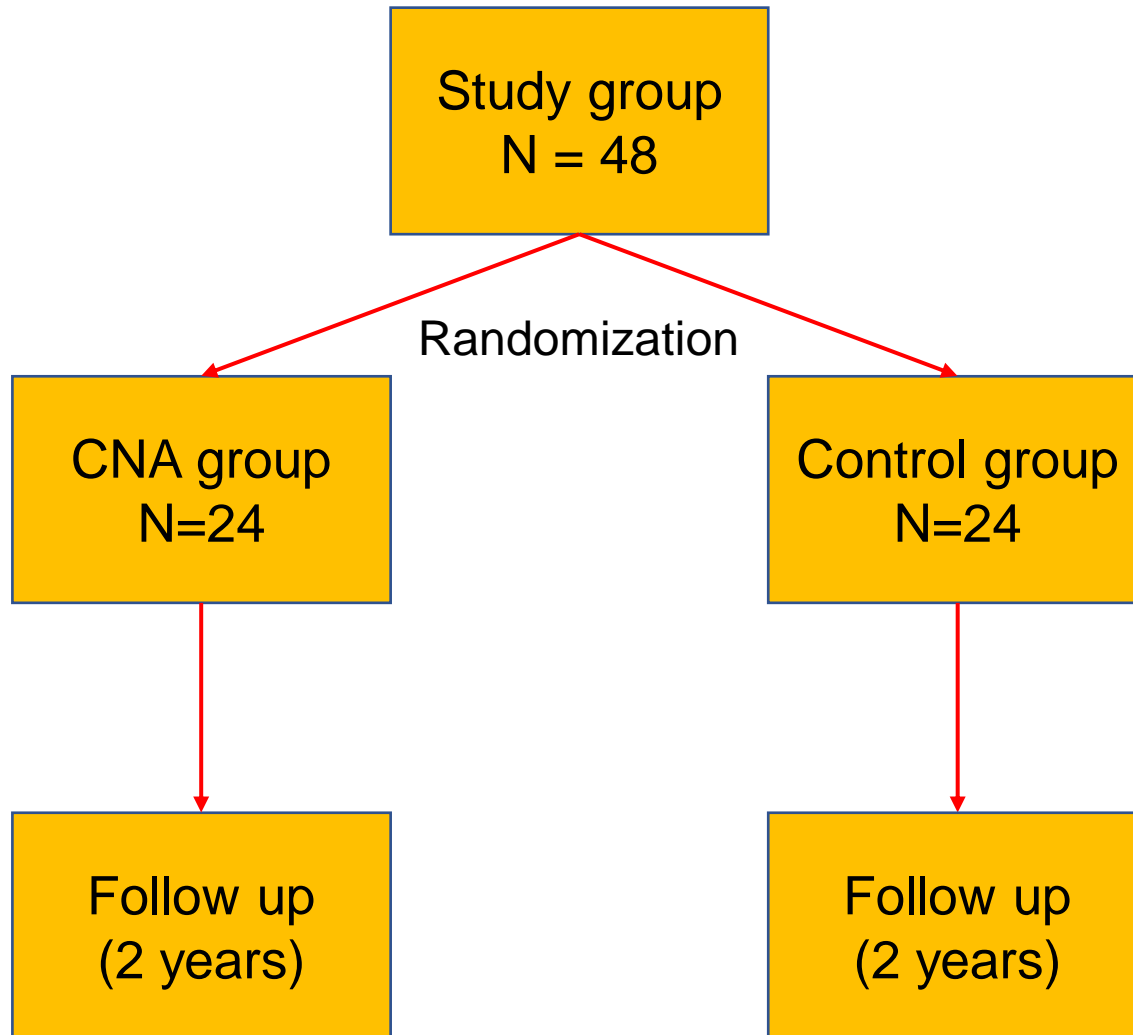
Cardioneuroablation for Reflex Syncope

Interim analysis

NIH U.S. National Library of Medicine

ClinicalTrials.gov

NCT03903744



Inclusion criteria

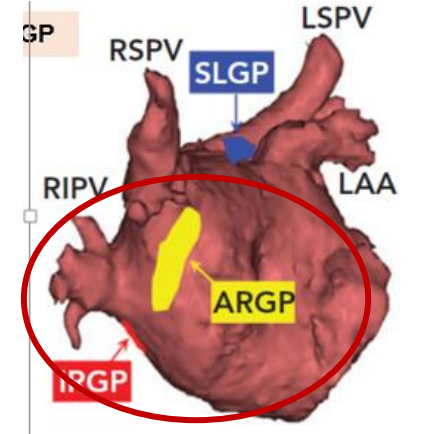
- At least one documented spontaneous VVS during preceding 12 months
- In case of lack of ECG documentation during spontaneous syncope - at least 3 s of asystole due to sinus arrest or atrio-ventricular block with syncope or bradycardia <40 beats per minute with syncope during baseline tilt test
- Sinus rhythm during ECG and tilt test
- Significantly decreased quality of life due to syncope
- Positive response to atropine challenge (\uparrow HR \geq 30% after atropine iv)
- Obtained written informed consent

Exclusion criteria

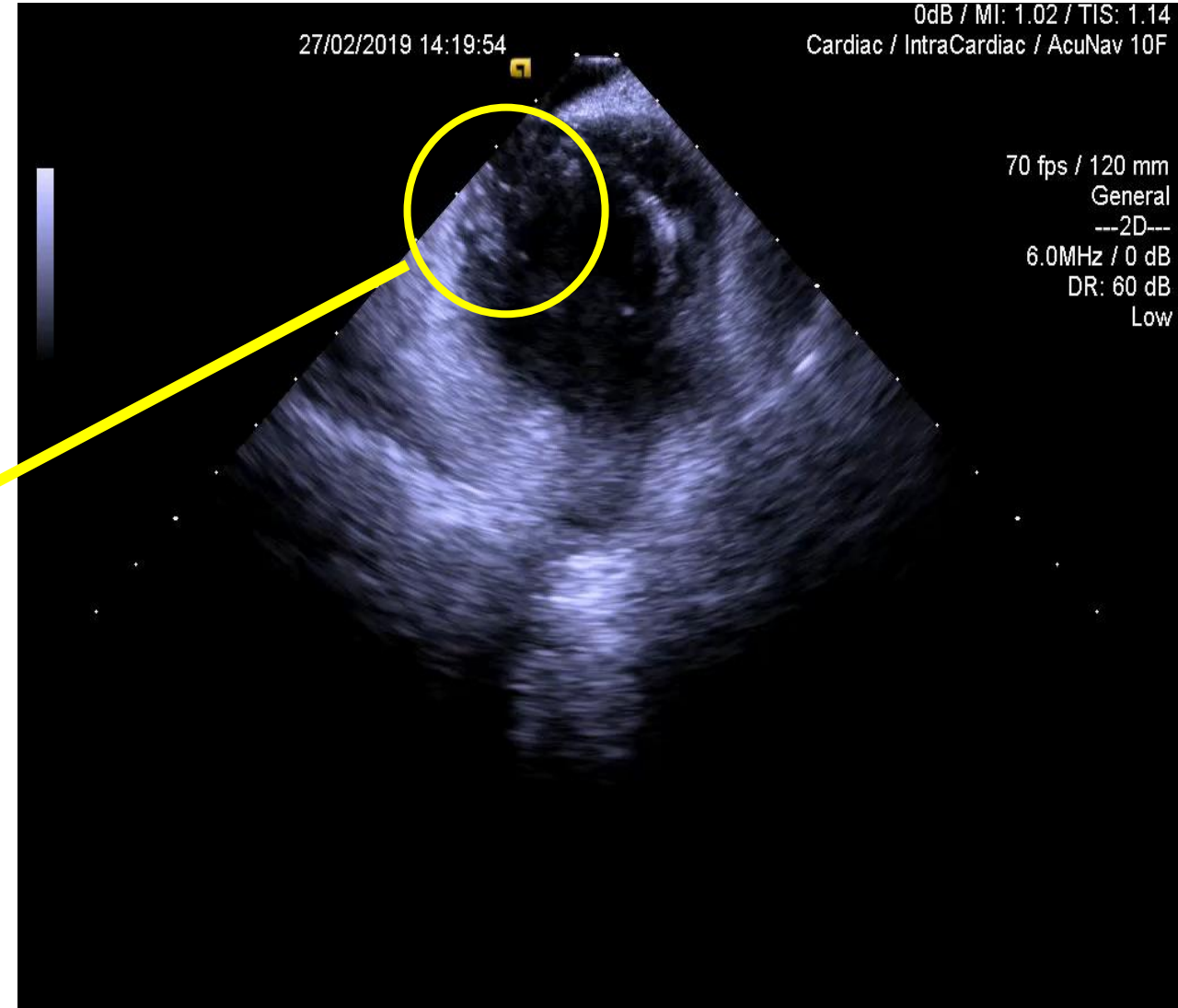
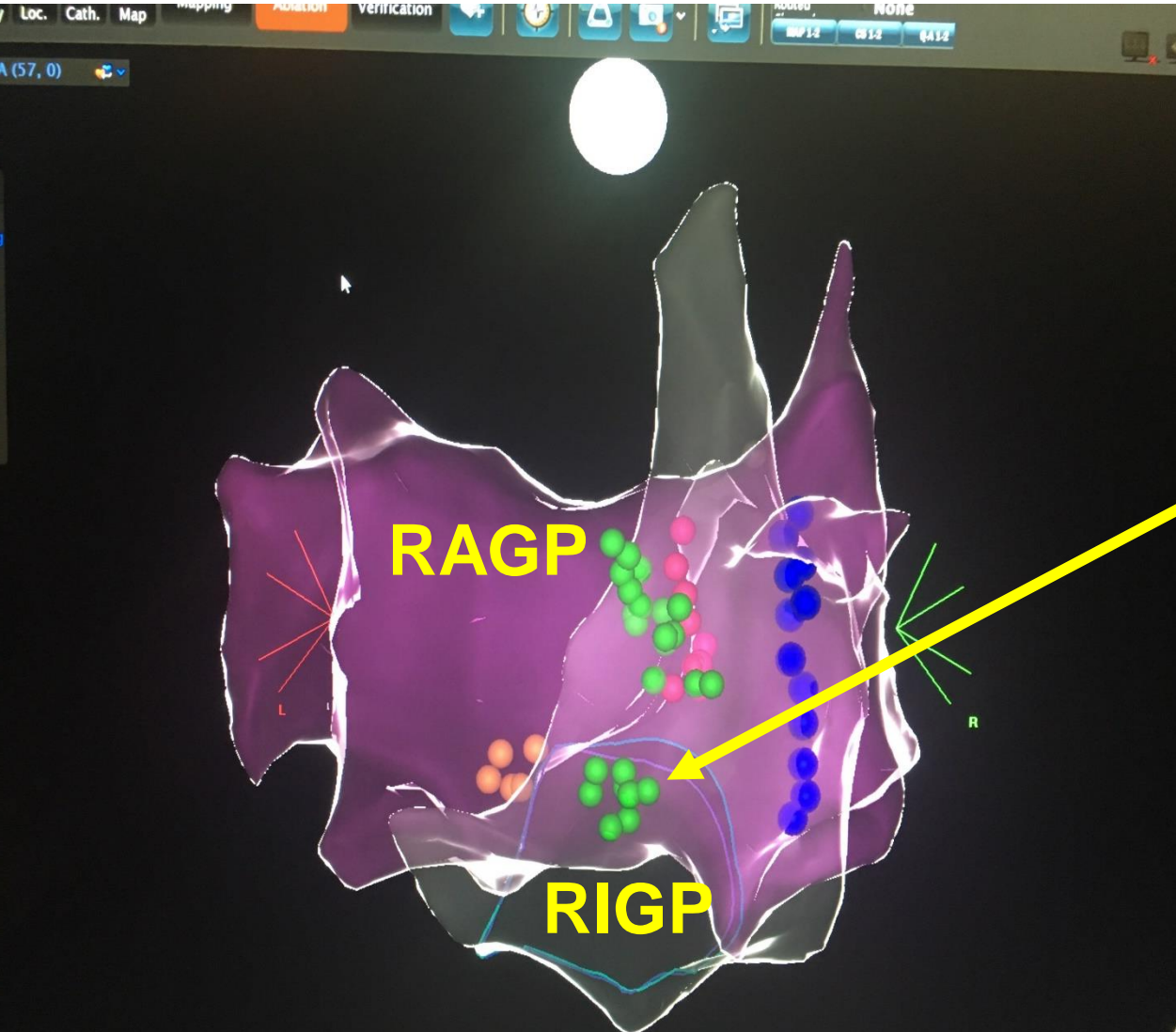
- Other possible and treatable causes of syncope such as significant cardiac disease, cardiac arrhythmia or abnormalities of vertebro-basilar arteries
- History of stroke or TIA
- History of cardiac surgery
- Contraindications to ablation in the right or left atrium
- Lack of response to atropine

Our approach

- **Procedure:** anatomic approach + fragmented electrogram ablation
 - Biatrial RAGP and RIGP
- **Endpoints** (before ECVS availability – since August 2020):
 - \uparrow HR ($>30\%$) (RAGP) and VR during RFA
 - \downarrow A-H, ERP AV, SNRT, cSNRT and WP
 - After CNA – response to atropine: \uparrow HR $<10\%$



RAGP and RIGP ablation



Demographic and clinical characteristics

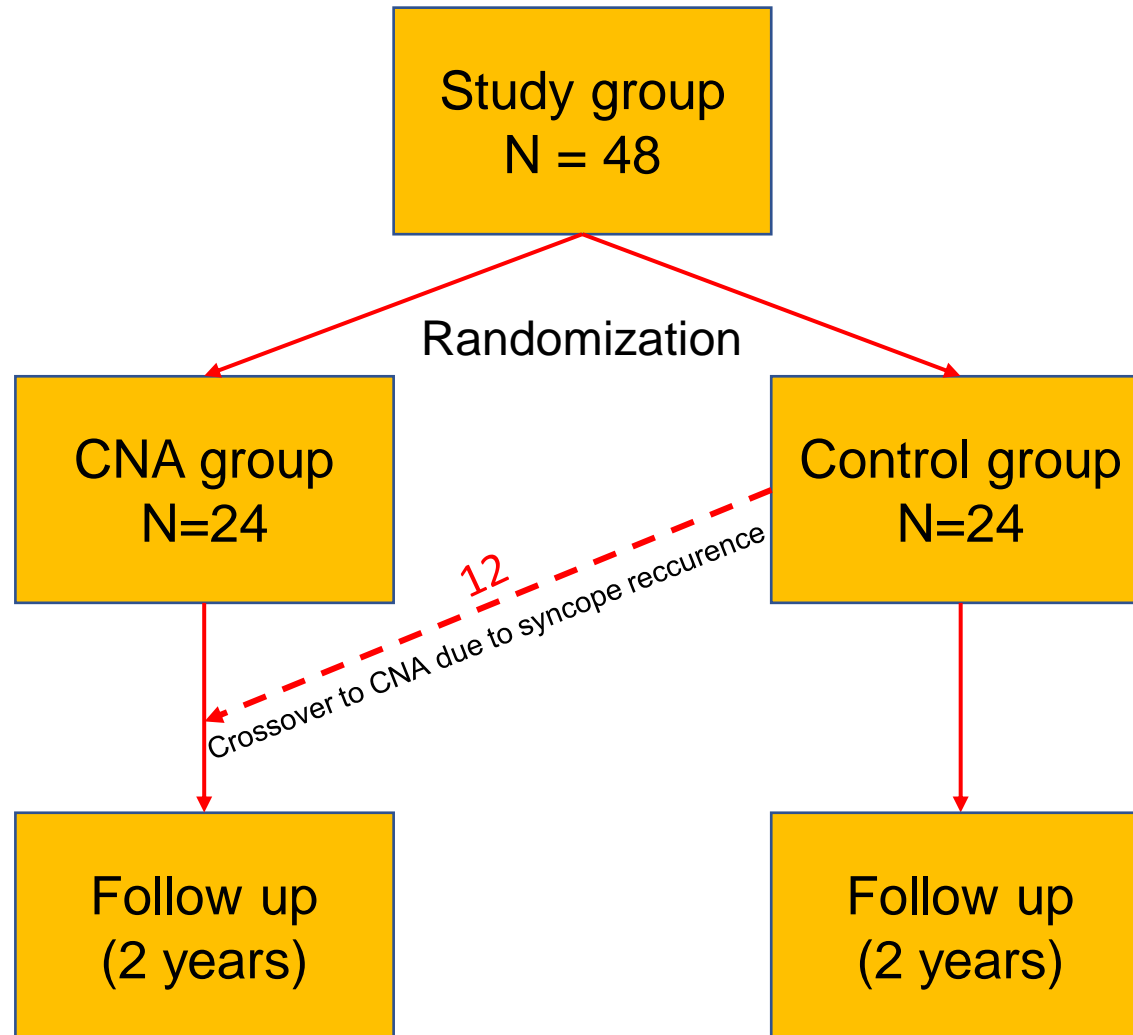
	CNA group	Control group	P
Number of pts.	24	24	NS
Age (years)	38 ± 10	37 ± 12	NS
Gender (Female / Male)	13 / 11	15 / 9	NS
Number of syncope in the preceding 12 months	3 ± 2	3 ± 3	NS

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➤ Primary endpoint: syncope recurrence

➤ Follow-up: 12 – 24 months

➤ CNA group: 1 syncope

➤ Control group: 12 syncope

P = 0.0007

➤ Final results: 2022

Our total CNA experience: 75 patients
PM explanted in 2 patients

Limitations and questions

- Placebo effect? Need for sham procedure?
- Acute end-points not well defined (ECVS, \uparrow HR, EP parameters, FEGM area ablated)
- Is total denervation really required?
- Optimal approach not established
- Long-term effectiveness not known
- Long-term safety not known
- Without above answers CNA should be still regarded as experimental procedure



Thank you for attention