# Il Futuro è nella Denervazione Simpatica


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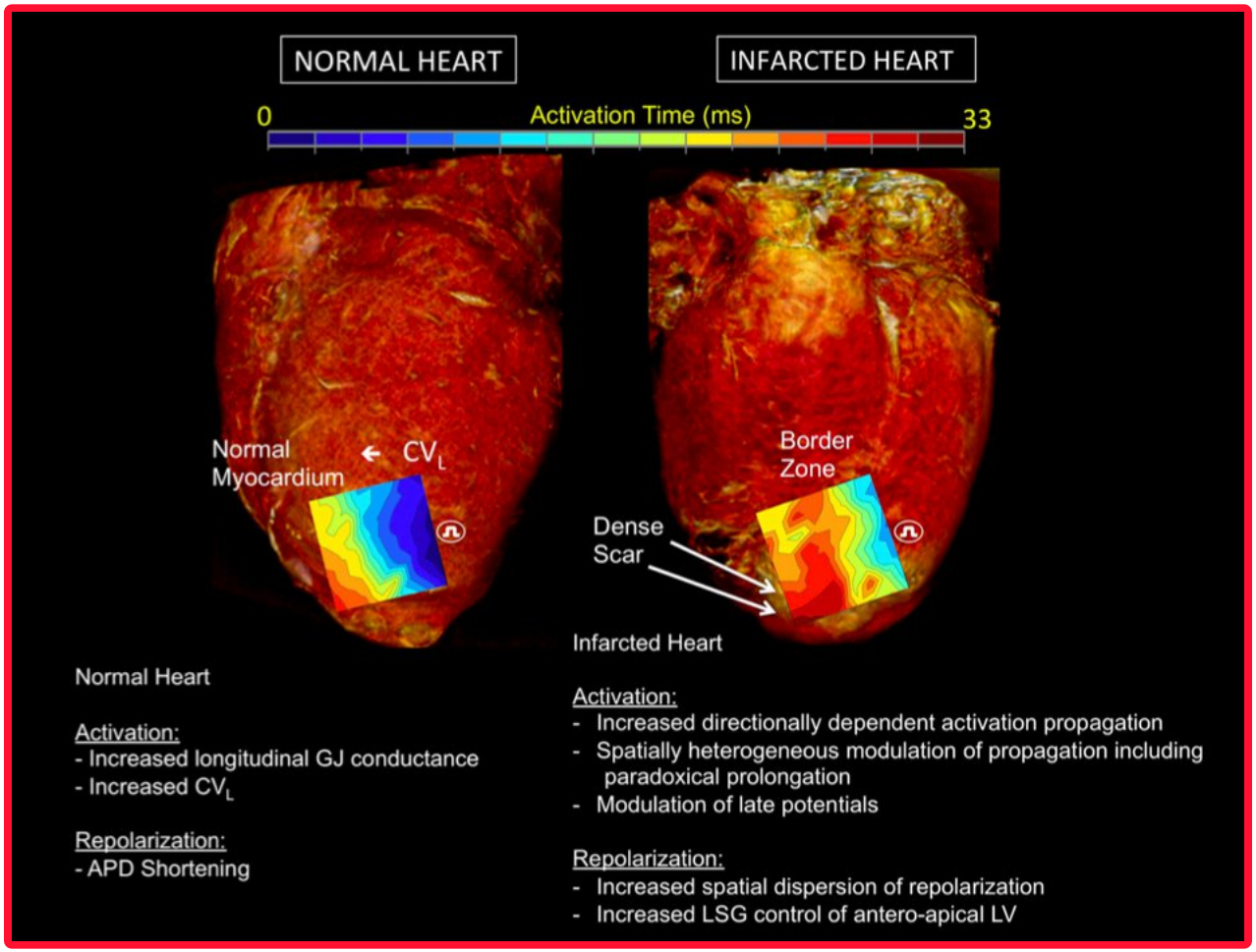
RESEARCH ARTICLE | *Cardiovascular Neurohormonal Regulation*

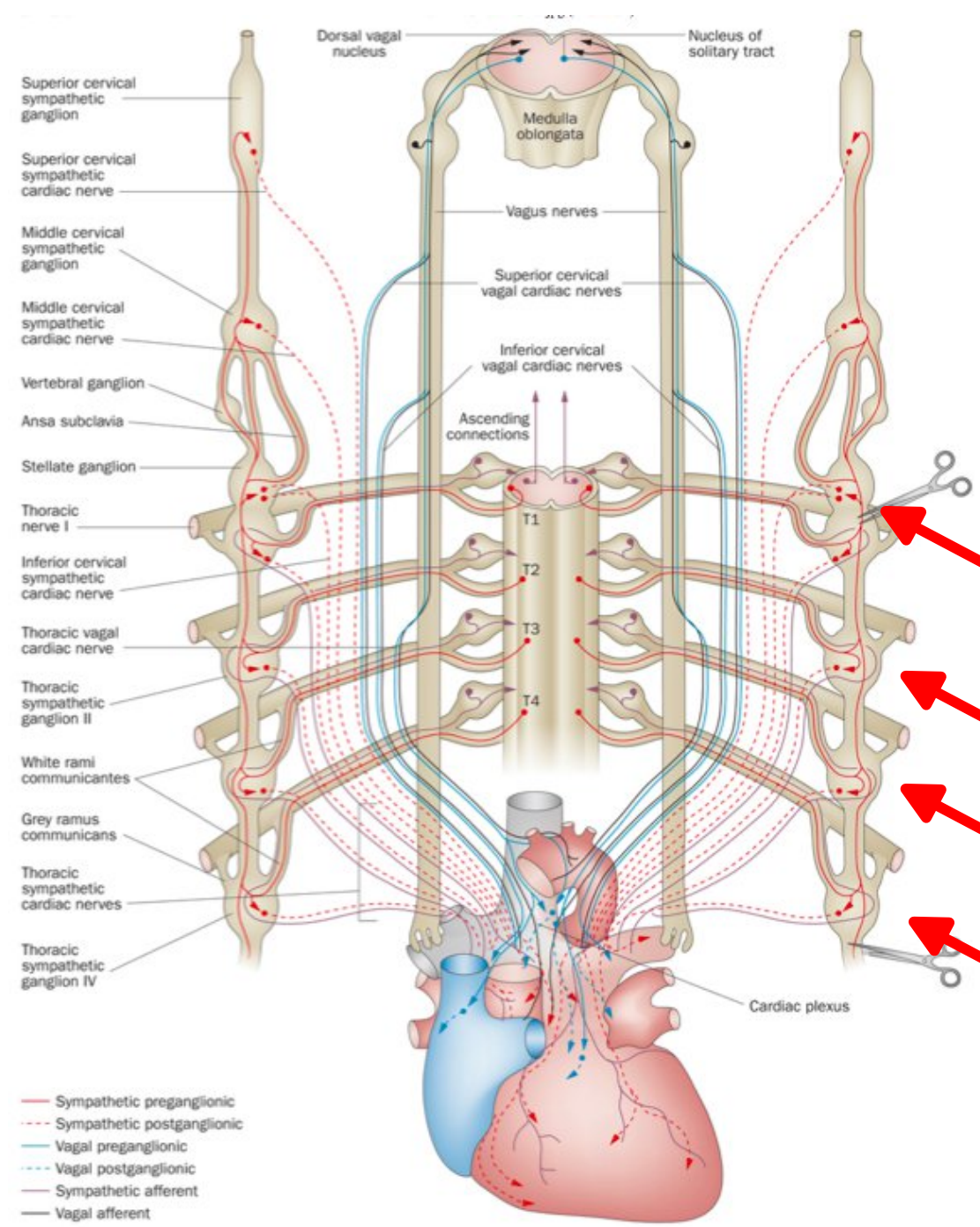
# Sympathetic modulation of electrical activation in normal and infarcted myocardium: implications for arrhythmogenesis

**Olujimi A. Ajijola,[1,2] Robert L. Lux,[5] Anadjeet Khahera,[1] OhJin Kwon,[1] Eric Aliotta,[3] Daniel B. Ennis,[3] Michael C. Fishbein,[4] Jeffrey L. Ardell,[1,2] and Kalyanam Shivkumar[1,2]**




*Am J Physiol Heart Circ Physiol 2017;312:H608–H621*

# Cardiac Sympathetic Denervation




**Stellate Ganglion**

**T2**

**T3**

**T4**

# Left Cardiac Sympathetic Denervation in the Management of High-Risk Patients Affected by the Long-QT Syndrome

Peter J. Schwartz, MD; Silvia G. Priori, MD, PhD; Marina Cerrone, MD; Carla Spazzolini, PhD; Attilio Odero, MD; Carlo Napolitano, MD, PhD; Raffaella Bloise, MD; Gaetano M. De Ferrari, MD; Catherine Klersy, MD, MS; Arthur J. Moss, MD; Wojciech Zareba, MD; Jennifer L. Robinson, MS; W. Jackson Hall, PhD; Paul A. Brink, MD; Lauri Toivonen, MD; Andrew E. Epstein, MD; Cuilan Li, MD; Dayi Hu, MD

(*Circulation*. 2004;109:1826-1833.)

# 147 HIGH RISK PATIENTS

Among ICD pts: 95% reduction of shocks

# Clinical Management of Catecholaminergic Polymorphic Ventricular Tachycardia

## The Role of Left Cardiac Sympathetic Denervation

Gaetano M. De Ferrari, MD*; Veronica Dusi, MD*; Carla Spazzolini, DVM, MS*; J. Martijn Bos, MD, PhD*; Dominic J. Abrams, MD, MRCP; Charles I. Berul, MD; Lia Crotti, MD, PhD; Andrew M. Davis, MB, BS, MD; Michael Eldar, MD; Maria Kharlap, MD; Asaad Khoury, MD; Andrew D. Krahn, MD; Antoine Leenhardt, MD; Christopher R. Moir, MD; Attilio Odero, MD; Louise Olde Nordkamp, MD; Thomas Paul, MD; Ferran Rosés i Noguer, MD; Maria Shkolnikova, MD; Jan Till, MD; Arthur A.M. Wilde, MD; Michael J. Ackerman, MD, PhD†; Peter J. Schwartz, MD†

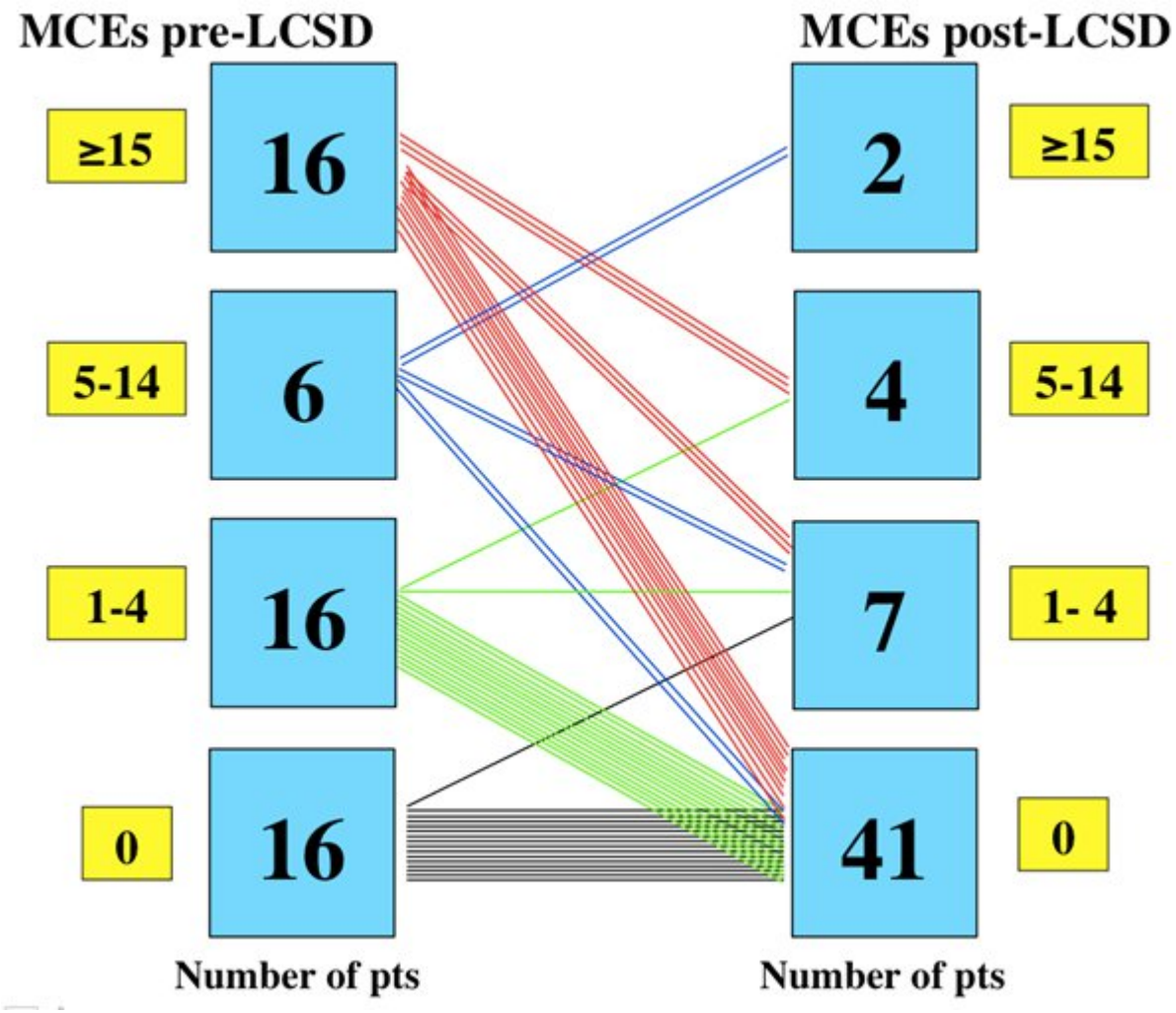
*Circulation*. 2015;131:2185-2193

# LCSD in Symptomatic CPVT Patients (16 without MCEs on OMT)

- 13 pts with MCEs after LCSD

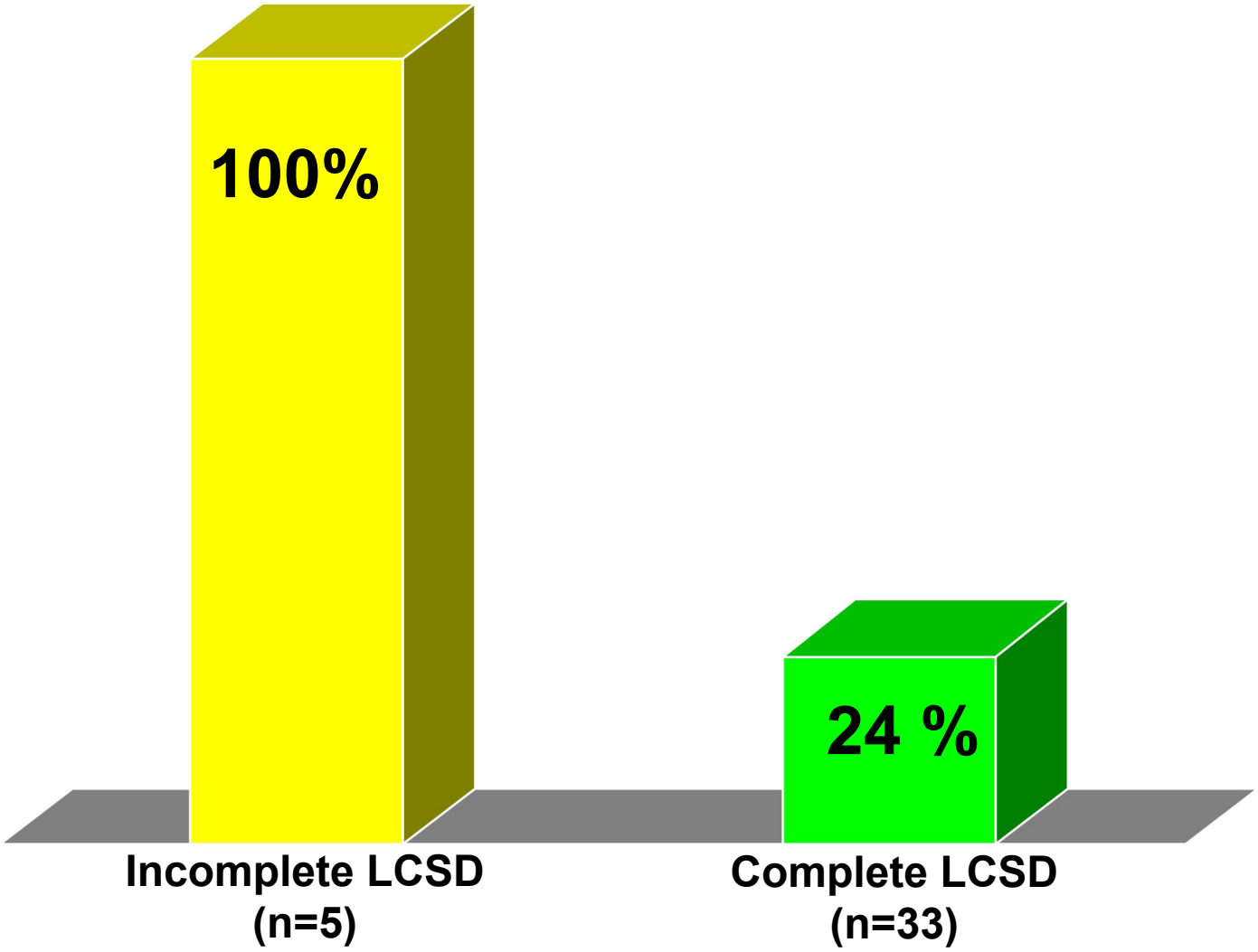
- 6 real non responders (1 sudden death)

- Mortality 1/54 (2%)



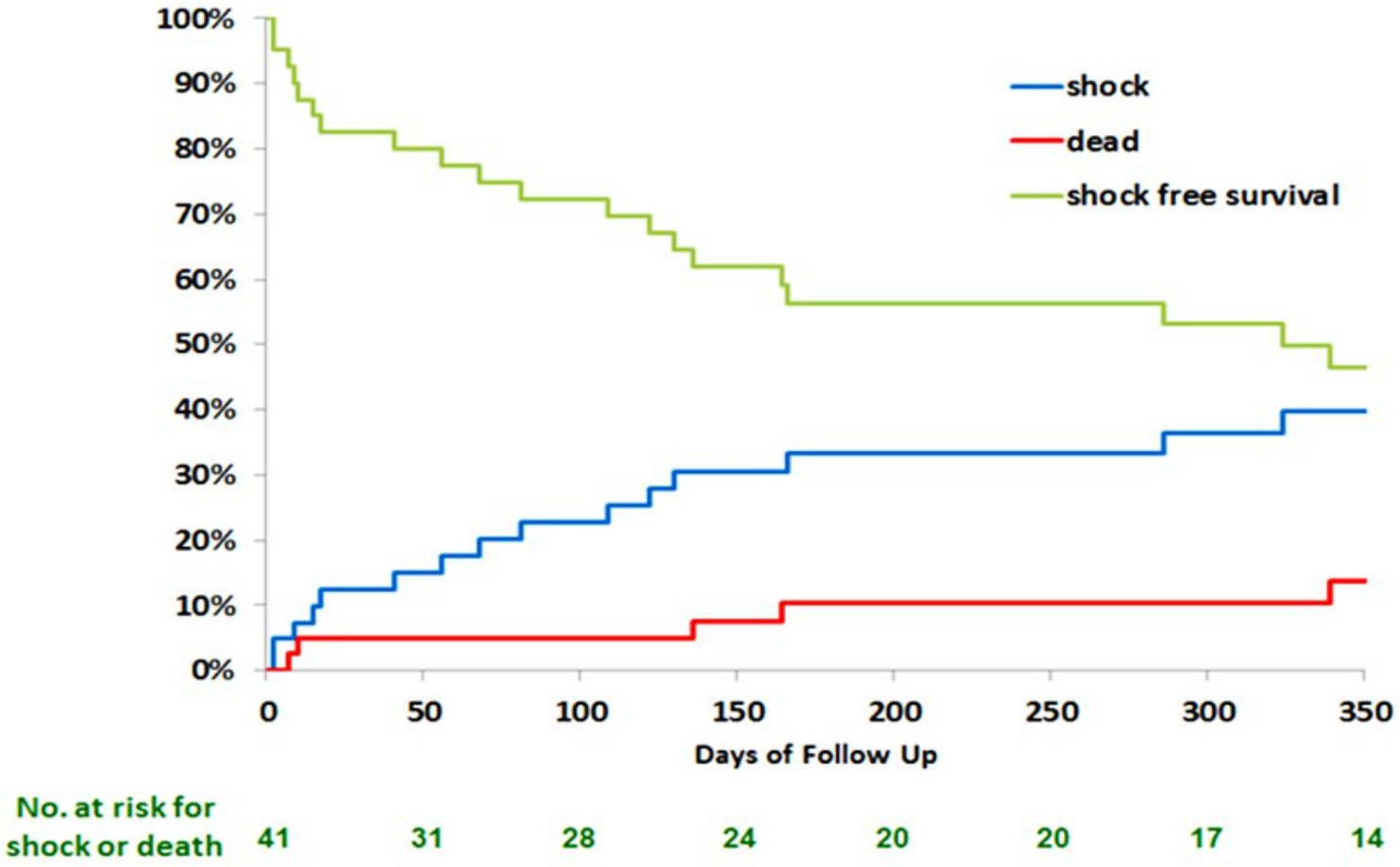

De Ferrari GM, et al. Circulation 2015;131:2185-93

# Dose-response Relationship of LCSD



# Structural Heart Disease
# Cardiomyopathies

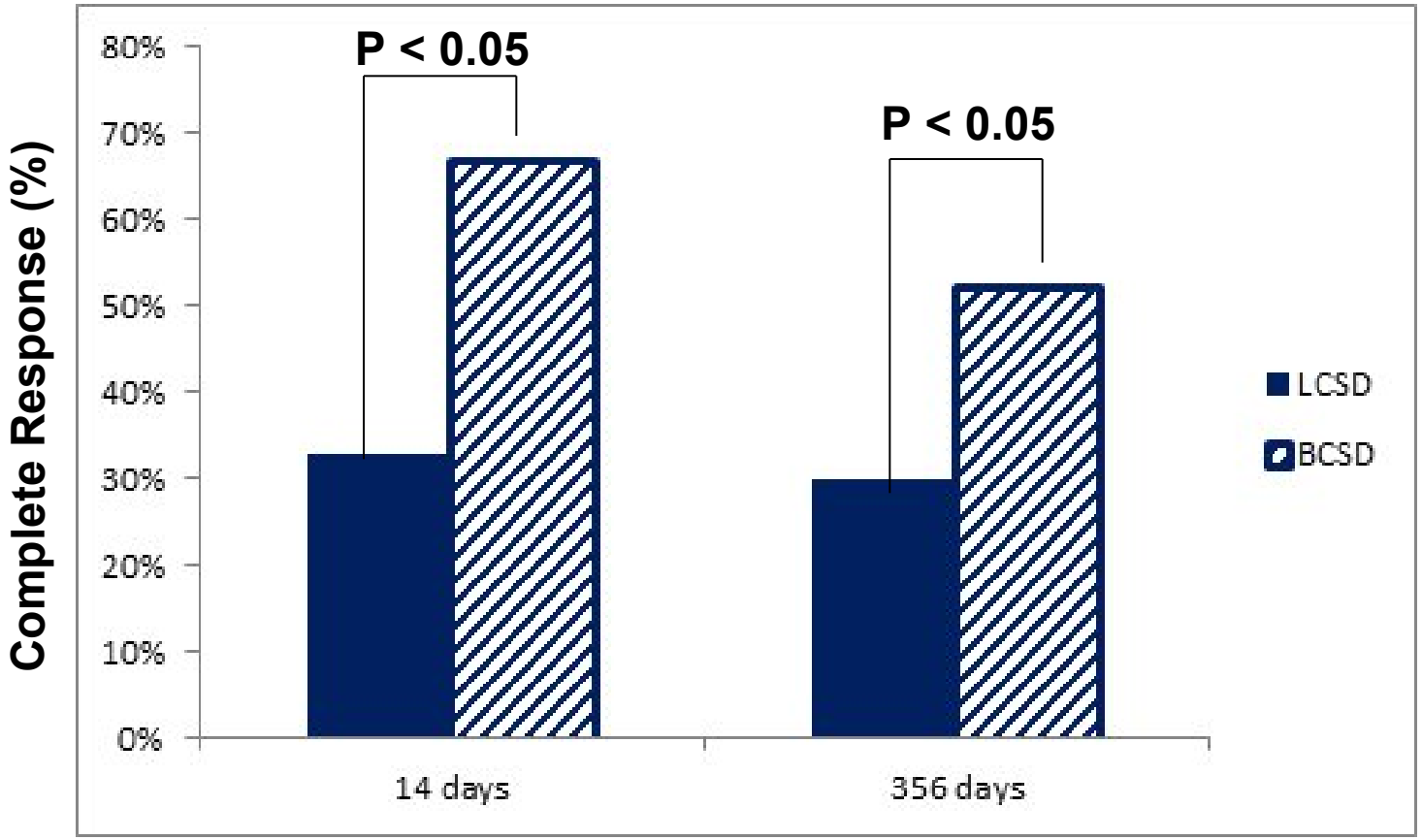
# Survival Free curves after CSD




**At mean follow-up of 367 ± 251 days (median 324 days), 17 patients (41%) died (10 in the LCSD and 7 in the BCSD group), mostly for HF.**

*Vaseghi M, et al. Heart Rhythm. 2014;11:360-366*

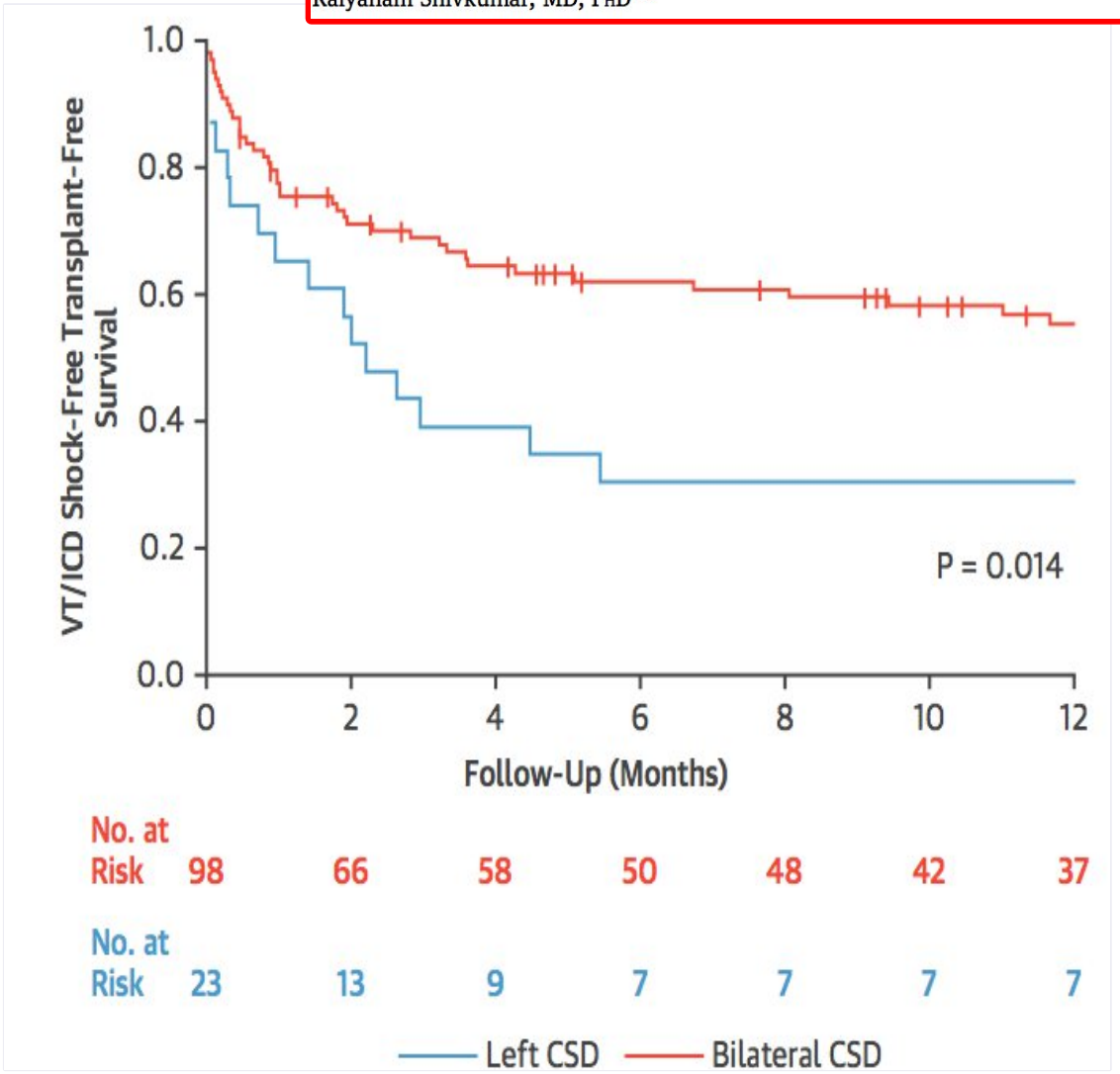
# CSD For VT & VF: Dose-response




*Vaseghi M, et al. Heart Rhythm. 2014;11:360-366*

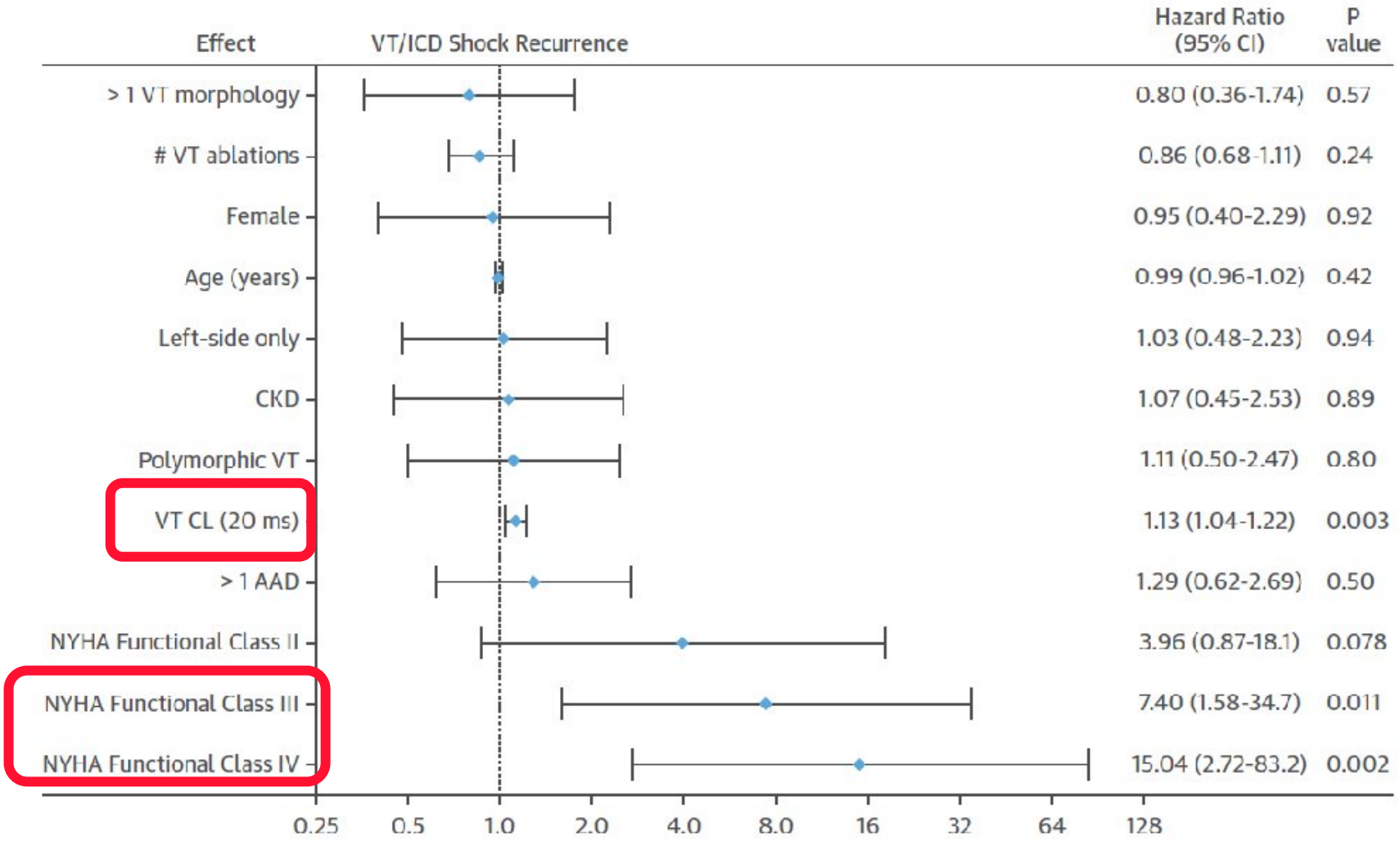
# Cardiac Sympathetic Denervation for Refractory Ventricular Arrhythmias

Marmar Vaseghi, MD, PhD,[a,b] Parag Barwad, MD, DM,[c] Federico J. Malavassi Corrales, MD,[d] Harikrishna Tandri, MD, MBBS,[e] Nilesh Mathuria, MD,[f] Rushil Shah, MBBS,[c] Julie M. Sorg, RN, MSN,[a] Jean Gima, RN, MSN, NP,[a] Kaushik Mandal, MD, MBBS,[e] Luis C. Sàenz Morales, MD,[d] Yash Lokhandwala, MD, DM,[c] Kalyanam Shivkumar, MD, PhD[a,b]




*J Am Coll Cardiol 2017;69:3070–80*

# Predictors of Recurrences after BCSD




*Vaseghi M et al J Am Coll Cardiol 2017;69:3070–80*

## Recurrent ventricular tachycardia after cardiac sympathetic denervation: Prolonged cycle length with improved hemodynamic tolerance and ablation outcomes

Justin Hayase MD | Veronica Dusi MD | Duc Do MD |
Olujimi A. Ajijola MD, PhD | Marmar Vaseghi MD, PhD | Jay M. Lee MD |
Jane Yanagawa MD | Nir Hoftman MD | Sha'Shonda Revels MD |
Eric F. Buch MD | Houman Khakpour MD | Osamu Fujimura MD |
Yuliya Krokhaleva MD | Carlos Macias MD | Julie Sorg RN, MSN |
Jean Gima RN, MSN, FNP-BC | Geraldine Pavez RN, MSN, ACNP-BC |
Noel G. Boyle MD, PhD | Kalyanam Shivkumar MD, PhD | Jason S. Bradfield MD

- 16 patients (94% males, 54 ± 13 years, 88% with NICM, LVEF 39± 10%) who underwent RFA for VT post-CSD (94% BCSD) were studied. A mean of 2.0 ± 0.8 RFAs for VT was unsuccessful before CSD.

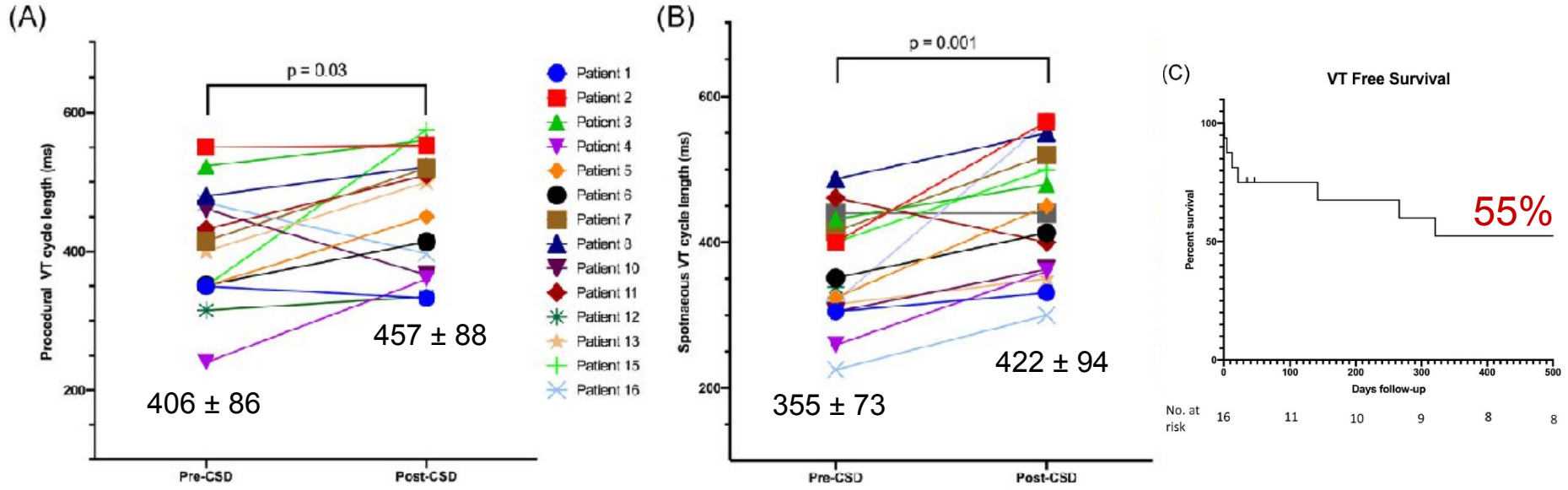
- The median time between CSD and post CSD RFA was 104 days (IQR 15–241).

- Hemodynamic tolerance was defined as the ability to perform activation mapping during the clinical VT without the use of mechanical circulatory support devices or additional sustained vasopressor agents during arrhythmia.

*J Cardiovasc Electrophysiol. 2020;31:2382–2392.*

# Recurrent ventricular tachycardia after cardiac sympathetic denervation: Prolonged cycle length with improved hemodynamic tolerance and ablation outcomes

- The clinical VT cycle length increased after CSD both spontaneously on ECG and/or ICD interrogation and intraprocedurally.
- Two patients had polymorphic and 14 had monomorphic VT (MMVT) pre-CSD, and all patients had MMVT post-CSD.
- **The proportion of mappable, hemodynamically stable VTs increased from 35% during pre-CSD RFA to 58% during post-CSD RFA (p = .038).**




*J Cardiovasc Electrophysiol. 2020;31:2382–2392.*

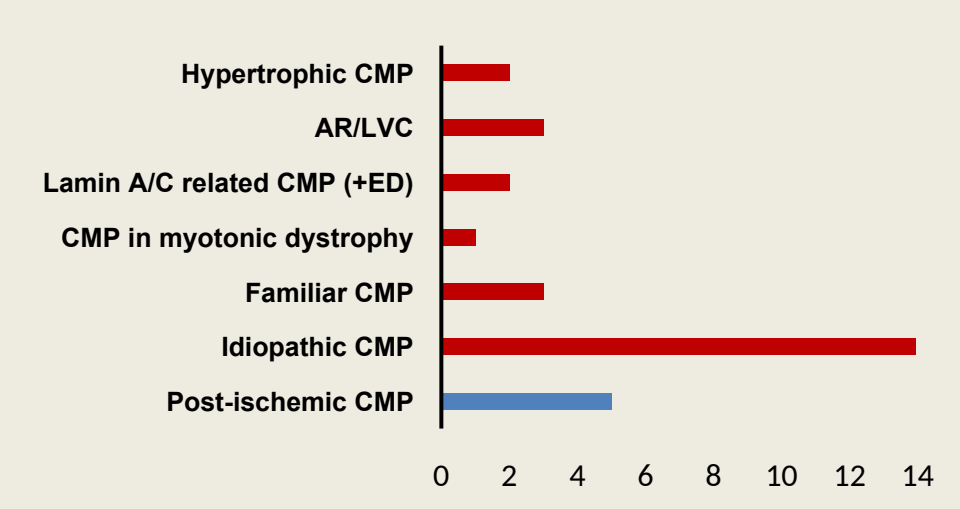
# Arrhythmic Risk Profile and Outcomes of Patients Undergoing Cardiac Sympathetic Denervation for Recurrent Monomorphic Ventricular Tachycardia After Ablation

Veronica Dusi, MD, PhD; Jeffrey Gornbein, DrPH; Duc H. Do, MD; Julie M. Sorg, RN, MSN; Houman Khakpour, MD; Yuliya Krokhaleva, MD; Olujimi A. Ajijola, MD, PhD; Carlos Macias, MD; Jason S. Bradfield, MD; Eric Buch, MD; Osamu A. Fujimura, MD; Noel G. Boyle, MD, PhD; Jane Yanagawa, MD; Jay M. Lee, MD; Kalyanam Shivkumar, MD, PhD; Marmar Vaseghi, MD, PhD

-36%

# Surgical Technique for BCSD VATS

# CSD in cardiomyopathies: Our experience (Pavia+Torino) since April 2016




**85% NICM (all types)**

| | |
|---|---|
| Male | 26, 87% |
| Mean age | 56 ± 16 (range 13-81) |
| LCSD | 4, 13% |
| ICD (all types) | 29, 97% |
| CRT-D | 11, 37 % |
| LVEF (%) | 31 ± 12, |
| NYHA Class I/II/III/IV (%) | 20/43/33/3 |
| VAD/OHT indication (for HF) | 9, 30% |
| History of electrical storm | 23, 77% |
| Chronic amiodarone | 18, 60% |
| Previous amiodarone-induced thyrotoxicosis | 5, 17% |
| Previous VT/PVC ablation | 14/2, 53% |
| Previous PLSGB | 5, 17% |
| pVT/fast VT (<250 msec) | 18, 60% |

**SAFETY:**

- Intra or peri-operatory (72 h) mortality: 0%
- Intra or peri-operatory (72) ECMO/Impella/IABP:0%
- Intra-operatory VT/VF: 1 case (slow VT), 3%

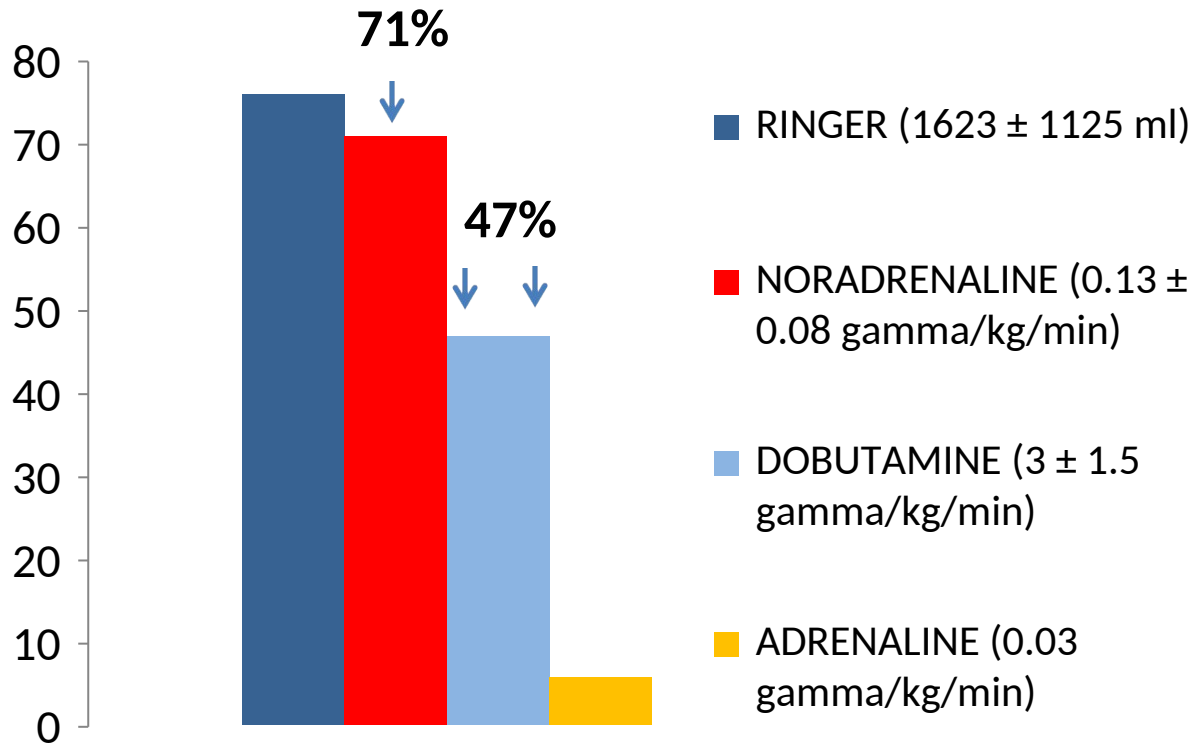
# Safety of BCSD in SHD: Intraprocedural data, n=17

**Procedural time**

**243 ± 64 min**

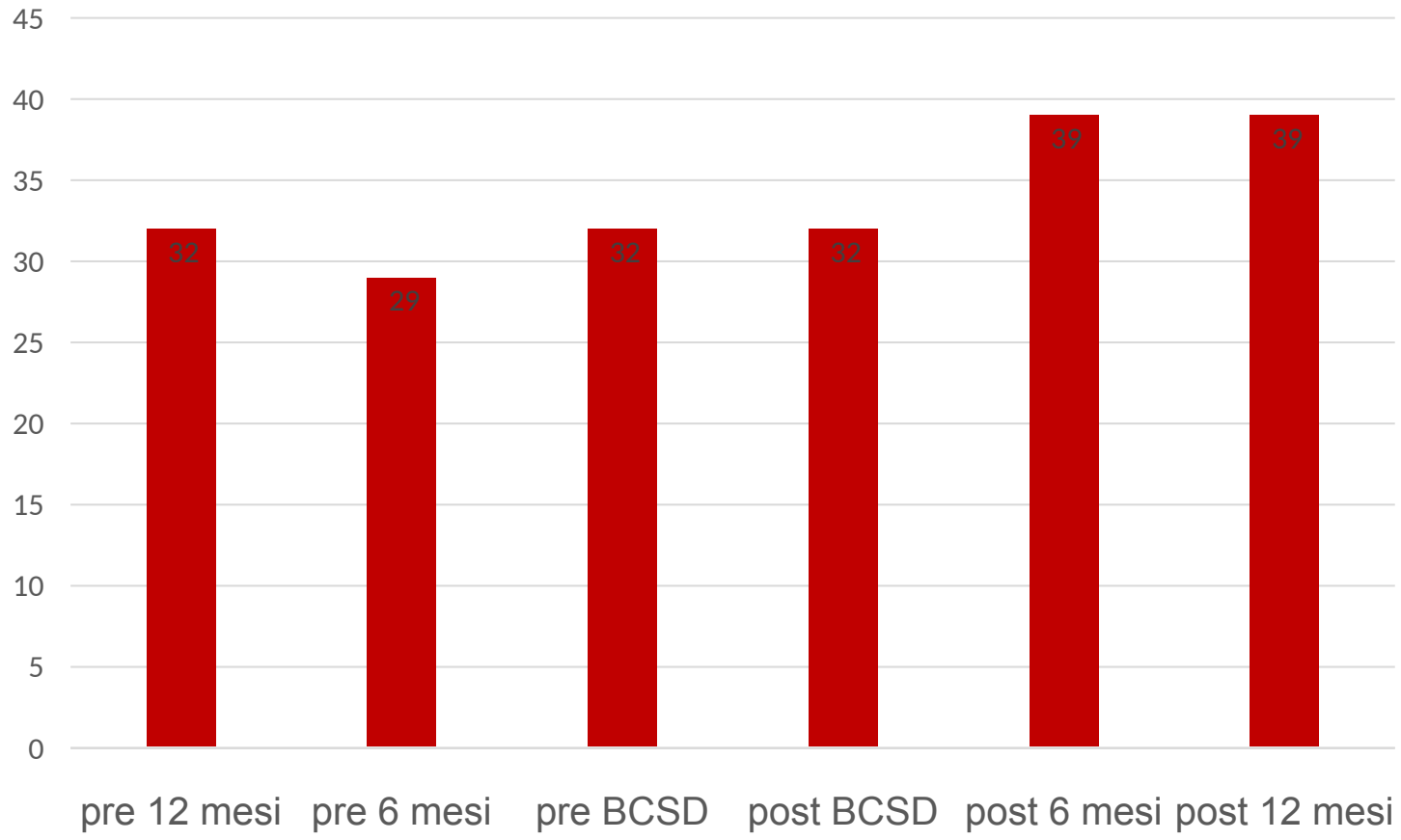
**Anesthesia time**

**318 ± 99 min**



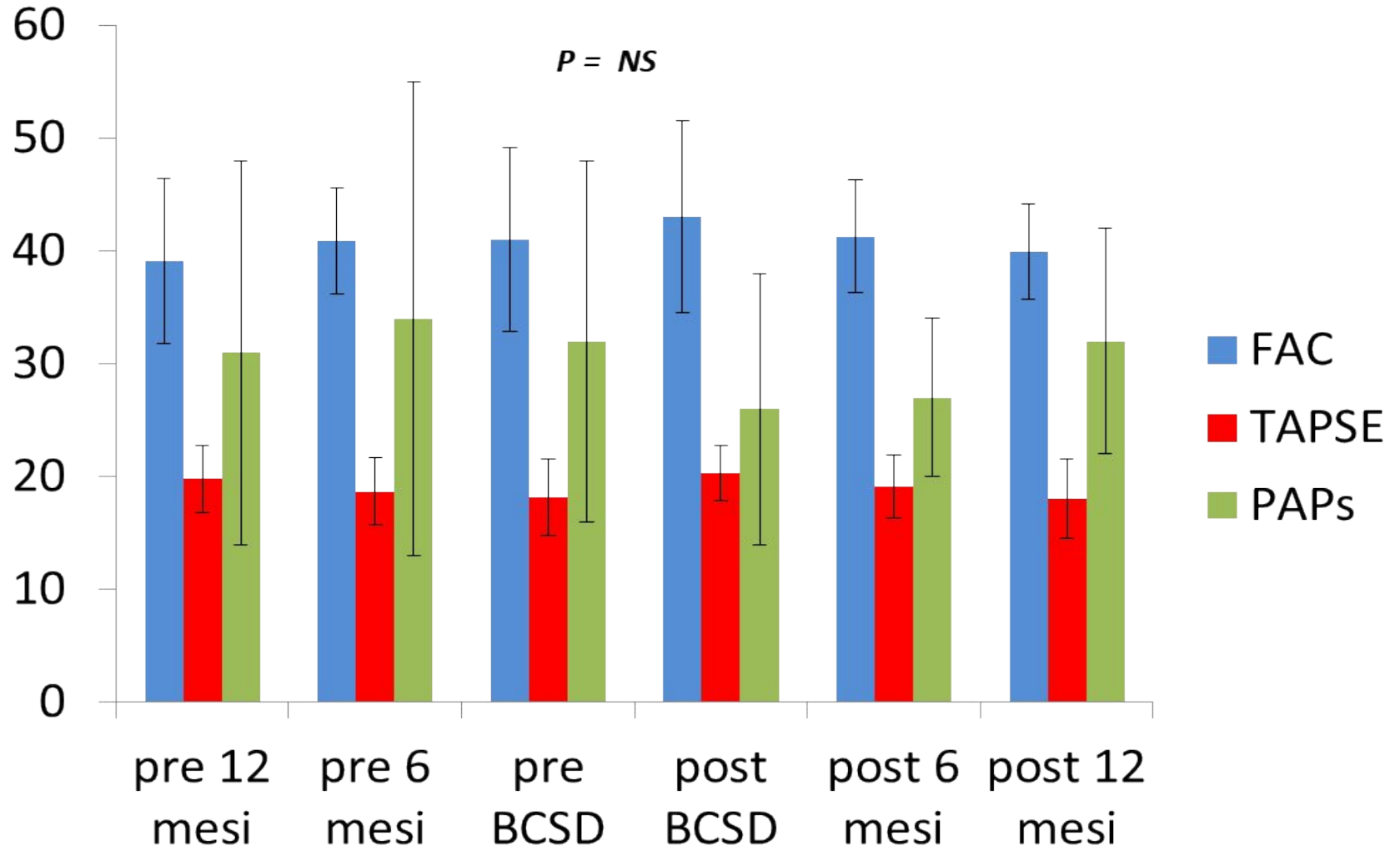

- No patients required advanced periprocedural heamodinamic support

# Safety of BCSD in SHD, n=17: Left Ventricular Ejection Fraction




P = ns for all comparisons

# Safety of BCSD in SHD, n=17: Right ventricular function




P = ns for all comparisons

# 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death


| | | |
|---|---|---|
| Autonomic modulation may be considered in patients with electrical storm refractory to drug treatment and in whom catheter ablation is ineffective or not possible.[326,328,340] | IIb | C |

# Conclusions

- CSD in patients with SHD has a strong pathophysiological rationale.
- Clinical efficacy data are limited but very promising, with no major safety concerns, when the procedure is performed in experienced centers.
- CSD should always be considered in patients with polymorphic VT/VF or rapid (HR>150 bpm) monomorphic VT on OMT and either not candidate and/or not responder to VT ablation.
- CSD may be considered in patients with ablation refractory monomorphic slow VT (HR <150 bpm), eventually combined with STAR to reduce the VT burden and the risk of ES.
- CSD should not be considered as an alternative to VT ablation, rather as a complementary strategy, particularly in case of complex and/or extensive and/or rapidly progressing substrates, to reduce the VT burden and the risk of ES and to improve the outcome of future VT ablation.

# Thank you for your attention

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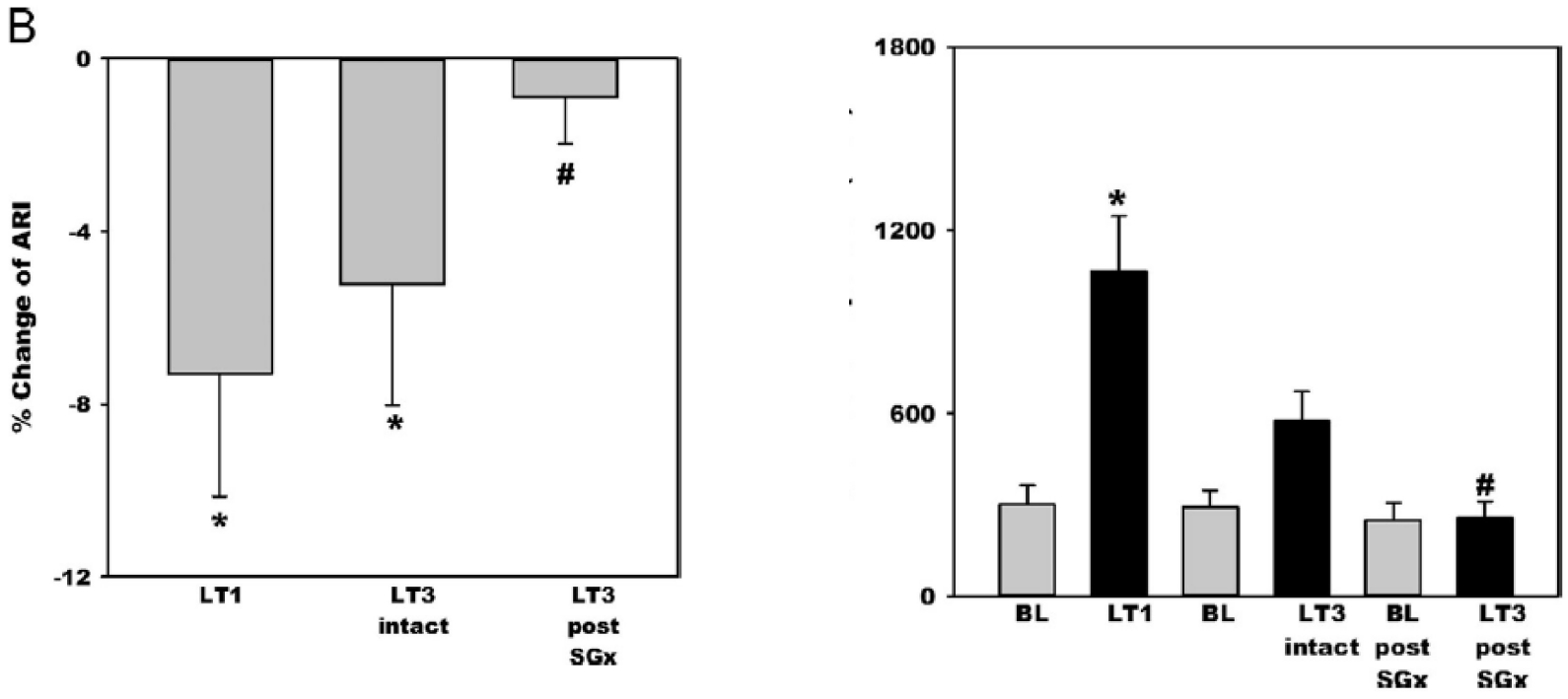
# Targeted stellate decentralization: Implications for sympathetic control of ventricular electrophysiology

Una Buckley, MD, Kentaro Yamakawa, MD, Tatsuo Takamiya, MD, J. Andrew Armour, MD, PhD, Kalyanam Shivkumar, MD, PhD, FHRS, Jeffrey L. Ardell, PhD




Heart Rhythm 2016;13:282–288

# Targeted stellate decentralization: Implications for sympathetic control of ventricular electrophysiology

Una Buckley, MD, Kentaro Yamakawa, MD, Tatsuo Takamiya, MD, J. Andrew Armour, MD, PhD, Kalyanam Shivkumar, MD, PhD, FHRS, Jeffrey L. Ardell, PhD

The results of this study demonstrate that removal of the lower third of T1 and the T2 paravertebral ganglia is sufficient to decentralize the sympathetic paravertebral ganglia from the heart with potentially less side effects.

Heart Rhythm 2016;13:282–288

# BCSD in specific SHD

**UCLA+ Bogota, 2016**

N = 7
All MMVT
Mn FU 7 months
57% freedom from ICD shock (all in the first months)

**Cardiac sympathetic denervation for intractable ventricular arrhythmias in Chagas disease**

Luis Carlos Saenz, MD, FHRS,* Federico Malavassi Corrales, MD,* William Bautista, MD,* Mahmoud Traina, MD,† Sheba Meymandi, MD,† Diego A. Rodriguez, MD, FHRS,* Luis J. Tellez, MD,* Marmar Vaseghi, MD, FHRS,‡ Fermin Garcia, MD,*§ Kalyanam Shivkumar, MD, PhD, FHRS,‡ Jason S. Bradfield, MD, FHRS†‡

**Johns Hopkins, 2019**

N = 8, 4 PKP2
FU 1.9 ± 0.9 yrs
63% freedom from recurrences

**Cardiac sympathectomy for refractory ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy**

Fabrizio R. Assis, MD,* Aravind Krishnan, BA,† Xun Zhou, MD,† Cynthia A. James, PhD,* Brittney Murray, MS,* Crystal Tichnell, MGC, RN,* Ronald Berger, MD, PhD, FHRS,* Hugh Calkins, MD, FHRS,* Harikrishna Tandri, MD,* Kaushik Mandal, MD, MPH, FHRS†

**Johns Hopkins, 2019**

N = 6, 5 BCSD
Mn FU 26 months (range 5-29)
100% freedom from ICD shock

**Cardiac sympathectomy for refractory ventricular arrhythmias in cardiac sarcoidosis**

David R. Okada, MD,* Fabrizio R. Assis, MD,* Nisha A. Gilotra, MD,* Jinny S. Ha, MD,† Ronald D. Berger, MD, PhD,* Hugh Calkins, MD,* Jonathan Chrispin, MD,* Kaushik Mandal, MD,† Harikrishna Tandri, MD*

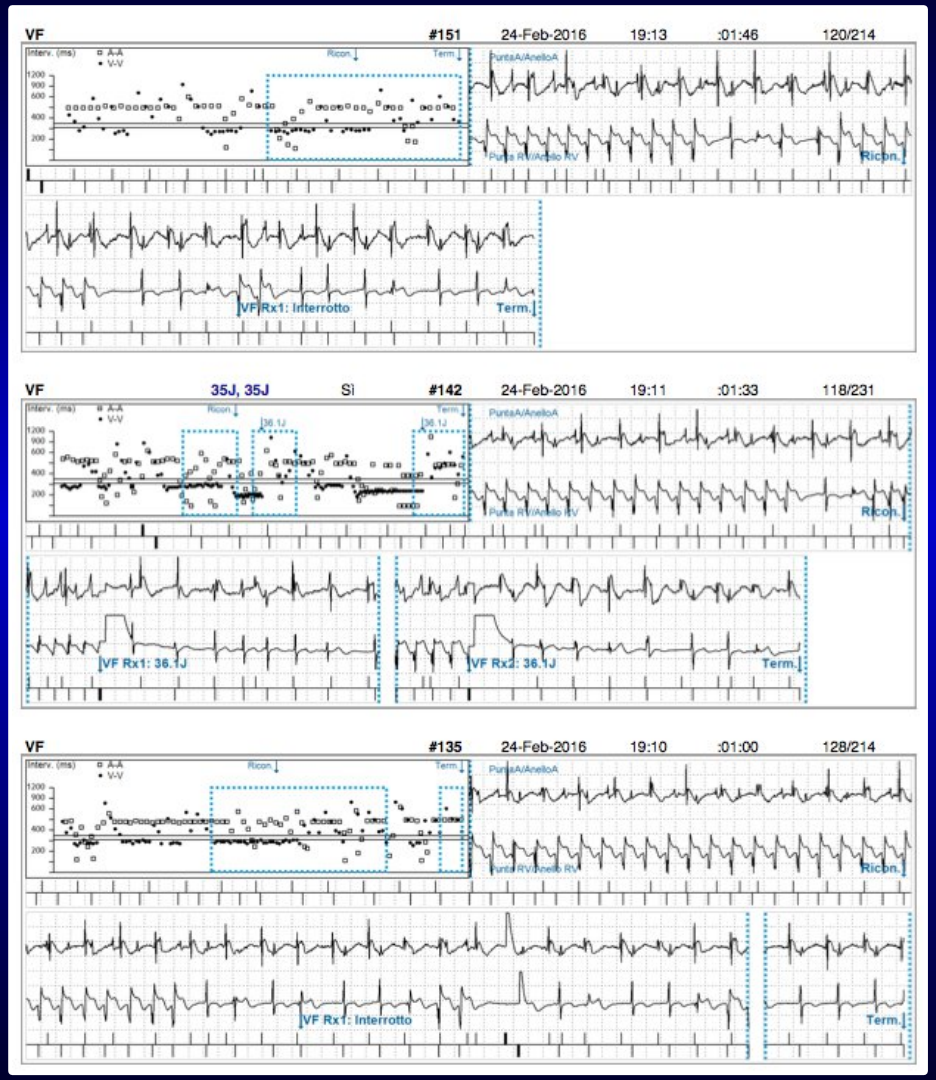
# Our first BCSD cases

- **Case 1, M, 44 yrs**: ES due to mVT in **ICM** despite chronic amiodarone + mexiletine and a previous endocardial VT ablation. Acute ventricular thrombus, LVEF 30-35% with apical aneurysm, NYHA I, dual chamber ICD. **BCSD: April 2016**

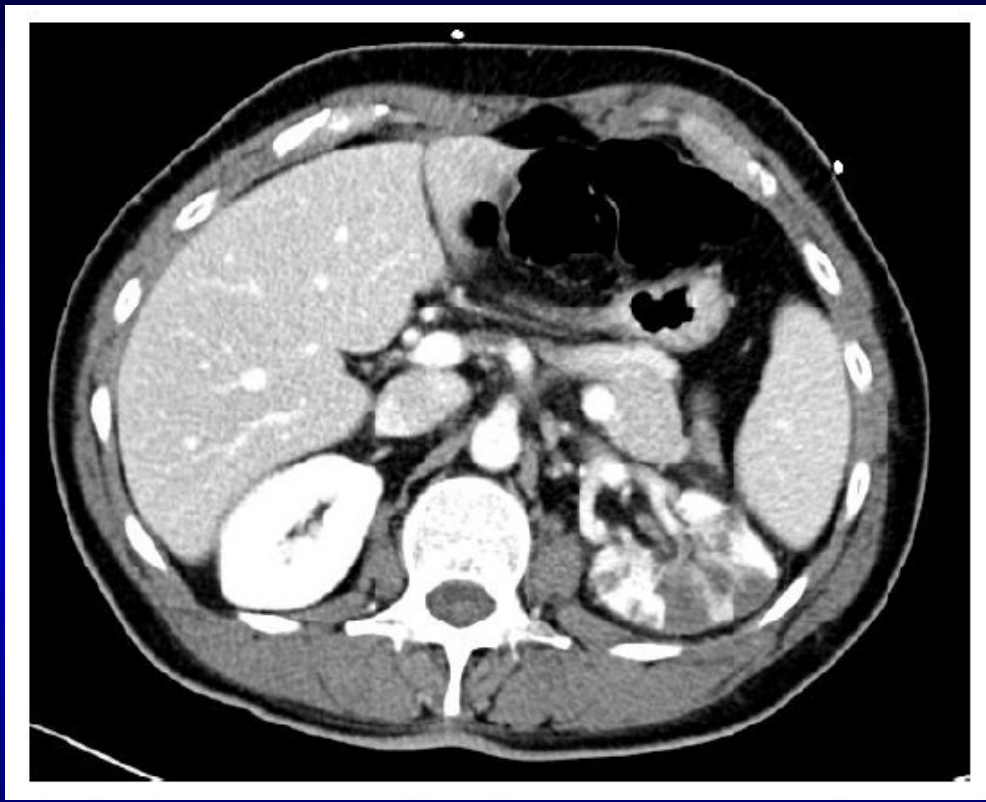
- **Case 2, F, 61 yrs:** ES due to pVT/VF in **NICM** despite BB+mexiletine, amiodarone controindication (autoimmune hyperthyroidism). LVEF 30%, NYHA IIb/III, CRT-D, heart transplant candidate (HTx).
- **BCSD: June 2016**

# Case 1, ICM: presentation

- **26 Feb 2016: severe electrical storm (74 shocks, 19 ATPs, several nsVT)**
- Recurrent monomorphic VT unresposive to ev amiodarone and lidocaine, slowly stabilized with ev procainamide
- Echo LVEDVi 105 ml/sqm, LVEF 30-35%, apical thrombus (3x2 cm)
- **…Few days after (10 Mar 2016) acute abdominal pain + creatinine increase….**

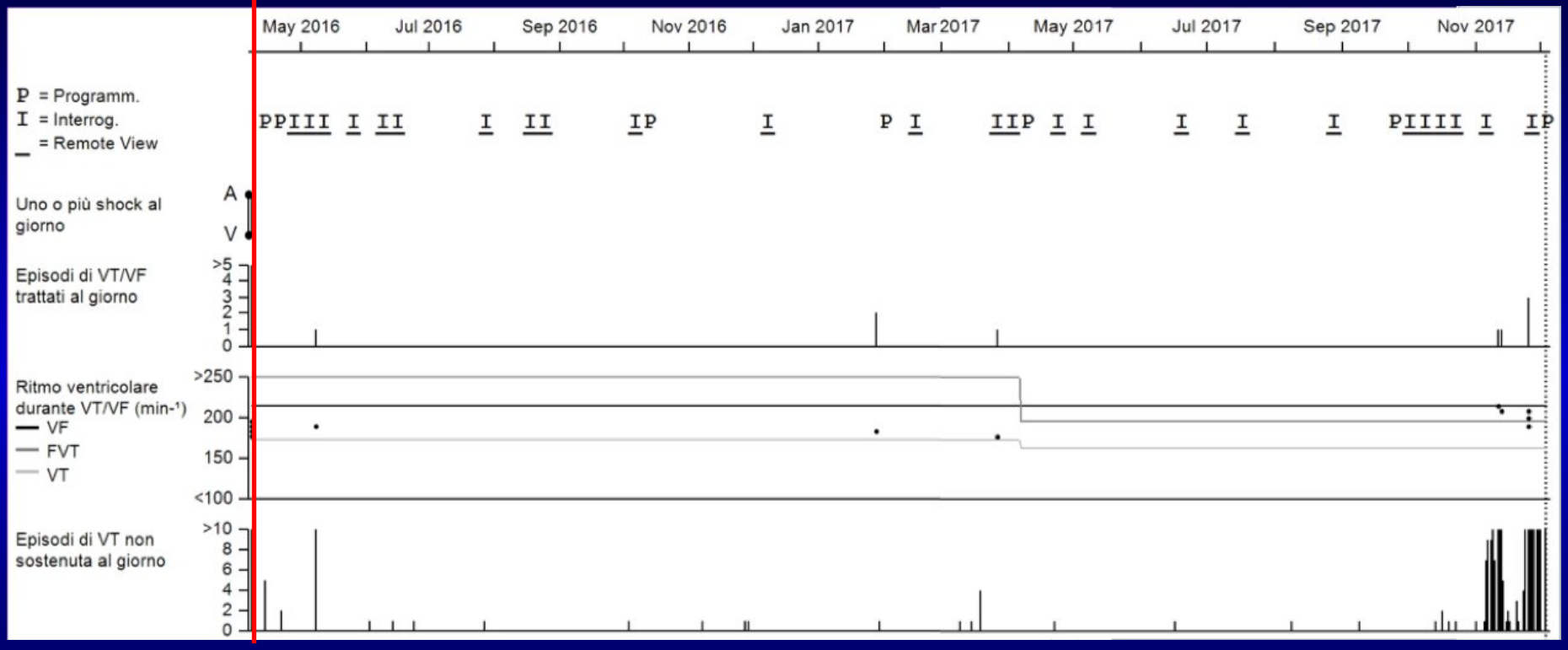


# Case 1, ICM: presentation



- 17 Mar 2016 mexiletine started (400 mg bid)
- **8 Apr 2016 ICD replacement**, in the night…**electrical storm** (6 ATP and relapsing nsTV), echo: apical thrombus (1x1 cm).

# Case 1: mVT in ICM (BCSD: 19 Apr 2016)




Post BCSD (19 months): no complication, mexiletine stopped (immediately), **echocardio stable,** NYHA I. Until november 2017 only 4 isolated ATP.

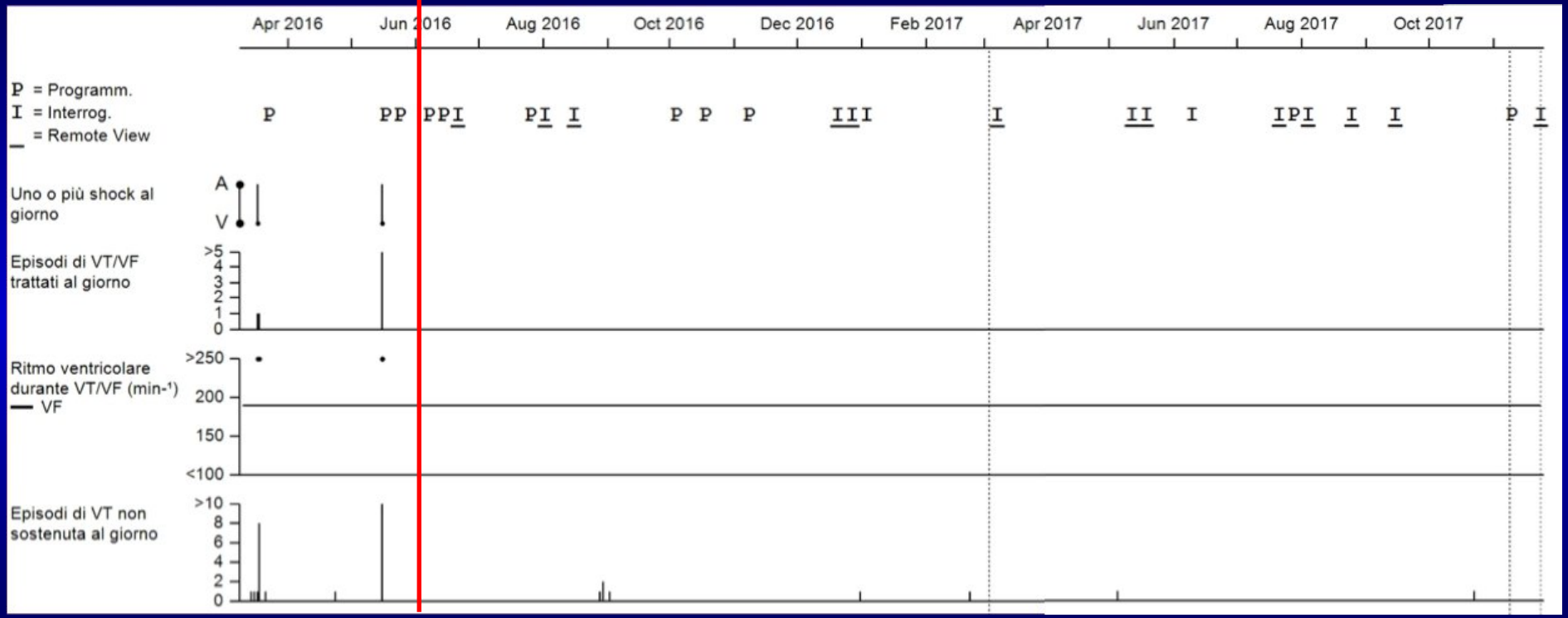
On novembre 2017 severe type 2 amiodarone - induced thyrotoxicosis, patient hospitalized but compltely asymptomatic despite very high burden of nsVT and PVC, only few ATP and 3 separate ICD shocks .

# Case 2, NICM: Presentation

| Tipo | ATP Seq | shock | Succ. | ID# | Data | Ora hh:mm | Durata hh:mm:ss | Media min-1 A/V | Max min-1 A/V |
|---|---|---|---|---|---|---|---|---|---|
| (Nessun dato dall'ultima sessione.) | | | | | | | | | |
| ---------- Ultima sessione programmatore 10-Jun-2016 ---------- | | | | | | | | | |
| VF | 0 | 35J | Sì | 69 | 16-May-2016 | 17:12 | :16 | 98/333 | - - -/--- |
| VF | 0 | 35J | Sì | 68 | 16-May-2016 | 17:09 | :27 | 118/400 | - - -/--- |
| VF | 0 | 35J | Sì | 67 | 16-May-2016 | 17:08 | :14 | 128/333 | - - -/353 |
| VF | 0 | 35J, 35J | Sì | 66 | 16-May-2016 | 17:07 | :27 | 128/286 | - - -/300 |
| VT-NS | | | | 65 | 16-May-2016 | 17:07 | :01 | 107/316 | |
| VF | 0 | 35J, 35J | Sì | 64 | 16-May-2016 | 17:06 | :28 | 125/353 | - - -/353 |
| VF | 0 | 35J | Sì | 63 | 16-May-2016 | 17:05 | :01:07 | 120/353 | - - -/353 |
| VT-NS | | | | 62 | 16-May-2016 | 17:05 | :01 | 120/222 | |
| VT-NS | | | | 61 | 16-May-2016 | 17:05 | :01 | 129/293 | |
| VT-NS | | | | 60 | 16-May-2016 | 17:04 | :01 | 130/214 | |
| VF | 0 | 35J, 35J | Sì | 59 | 16-May-2016 | 17:03 | :27 | 136/353 | - - -/353 |
| VF | 0 | 35J | Sì | 58 | 16-May-2016 | 17:02 | :21 | 128/375 | - - -/--- |
| VT-NS | | | | 57 | 16-May-2016 | 17:01 | :01 | 130/258 | |
| VT-NS | | | | 56 | 16-May-2016 | 17:01 | <:01 | 133/250 | |
| VT-NS | | | | 55 | 16-May-2016 | 17:00 | :04 | 138/286 | |
| VT-NS | | | | 54 | 16-May-2016 | 17:00 | :02 | 135/252 | |
| VF | 0 | | | 53 | 16-May-2016 | 16:59 | :11 | 133/300 | - - -/--- |
| VT-NS | | | | 52 | 16-May-2016 | 16:59 | :01 | 124/250 | |
| VT-NS | | | | 51 | 16-May-2016 | 16:58 | :02 | 118/279 | |
| VT-NS | | | | 50 | 16-May-2016 | 16:58 | :01 | 98/240 | |
| VT-NS | | | | 49 | 16-May-2016 | 16:41 | :06 | 113/287 | |
| VT-NS | | | | 48 | 16-May-2016 | 16:40 | :02 | 110/300 | |
| VT-NS | | | | 47 | 16-May-2016 | 16:39 | :02 | 117/267 | |
| VT-NS | | | | 46 | 16-May-2016 | 16:38 | :03 | 128/269 | |
| SVT-TS | | | | 45 | 16-May-2016 | 16:38 | :43 | 140/140 | 140/140 |
| VF | 0 | 35J | Sì | 44 | 16-May-2016 | 16:37 | :24 | 167/375 | ---/375 |
| VF | 0 | 35J | Sì | 43 | 16-May-2016 | 16:36 | :29 | 136/300 | - - -/300 |
| VF | 0 | 35J | Sì | 41 | 16-May-2016 | 16:33 | :13 | 109/462 | - - -/--- |
| VF | 0 | | | 40 | 16-May-2016 | 16:31 | :12 | 115/214 | - - -/250 |

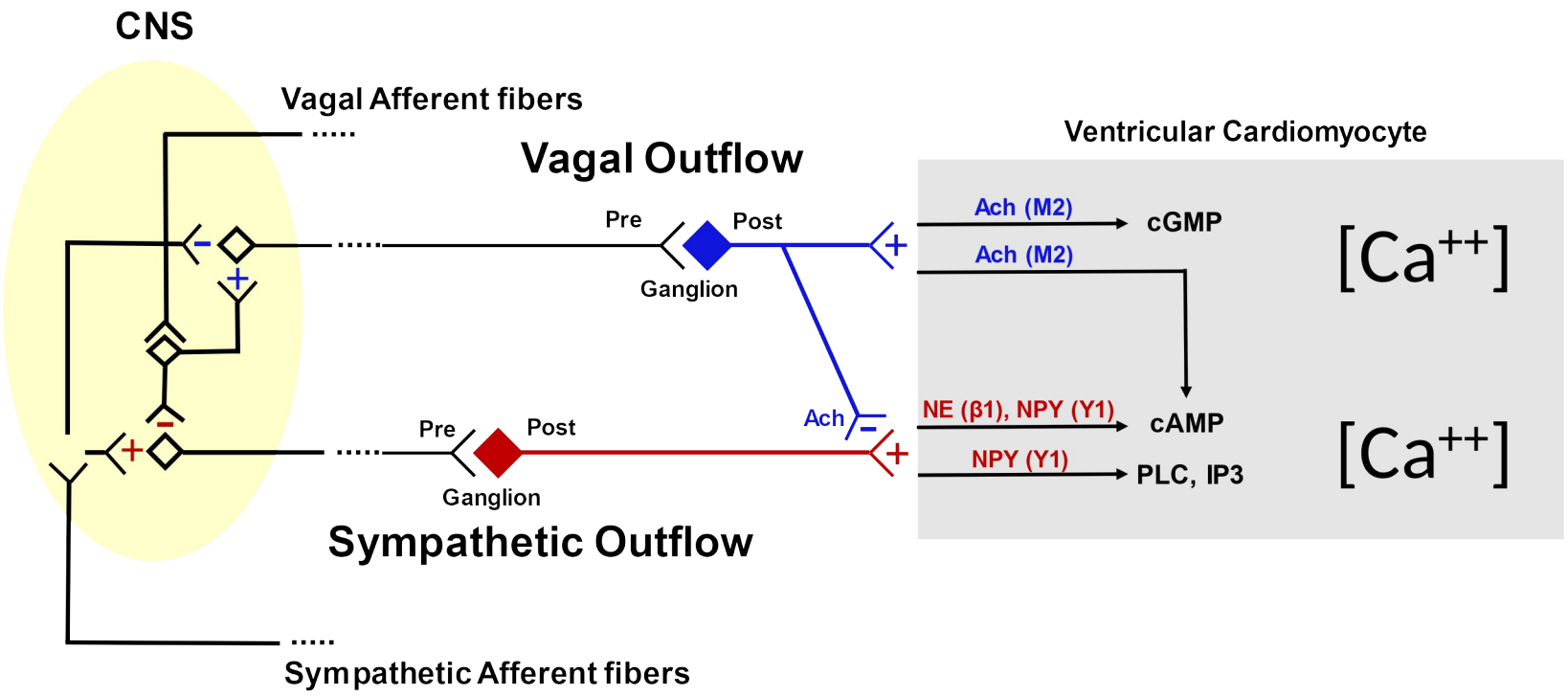
- **16 May 2016 second electrical storm: 14 ICD shocks on pVT/VF in less than 1 hour.**
- She was treated with ev amiodarone on the ambulance (total 450 mg in about 30 minutes)
- No triggering/precipitating factors

# Caso 2 pVT/VF in NICM (BCSD: 3 June 2016)




Post BCSD: neuropathic pain lasting about 3 months, mexiletine stopped (immediately), sporadic polimorphic NSVT, echocardio and cardiac catheterization stable, better functional status (NYHA II stable), no hospitalization for AHF

# Sympatho-vagal Interaction



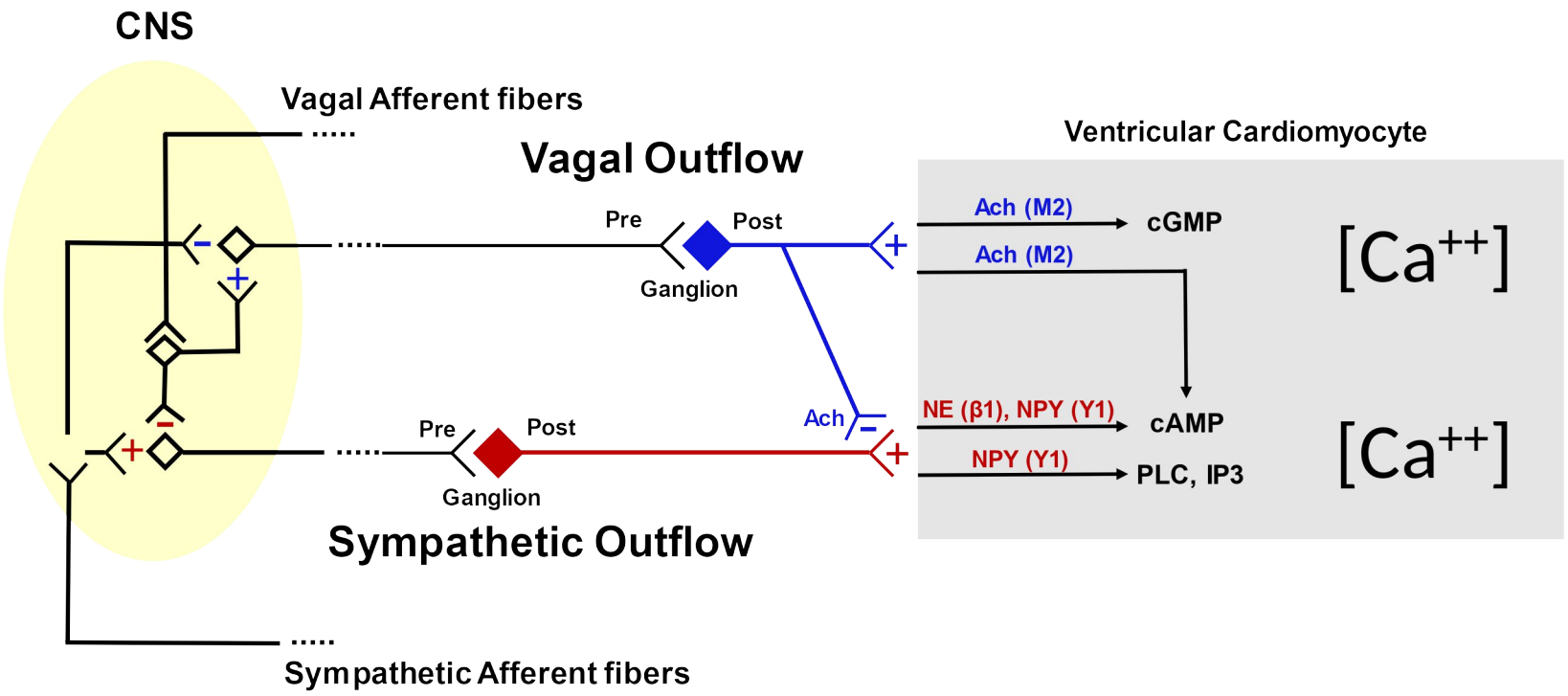

To obtain a net decrease of sympathetic effects at the cardiac level we may either

- Decrease sympathetic outflow or
- Increase vagal input and/or ouput

} **Neuromodulation**

*V. Dusi, et al EHJ 2020, doi: 10.1093/eurheartj/ehz950.*

# Sympatho-vagal Interaction

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} **Neuromodulation**

*V. Dusi, et al EHJ 2020, doi: 10.1093/eurheartj/ehz950.*