Learning Objectives to Disclose:

- To **CRITIQUE** the ICD and its role in the treatment of BrS, CPVT, and LQTS

MAYO CLINIC

WINDLAND SMITH RICE
SUDDEN DEATH
GENOMICS LABORATORY

Conflicts of Interest to Disclose:

- Consultant – Boston Scientific, Gilead Sciences, Medtronic, St. Jude Medical, and Transgenomic/FAMILION
- Royalties – Transgenomic/FAMILION

Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes

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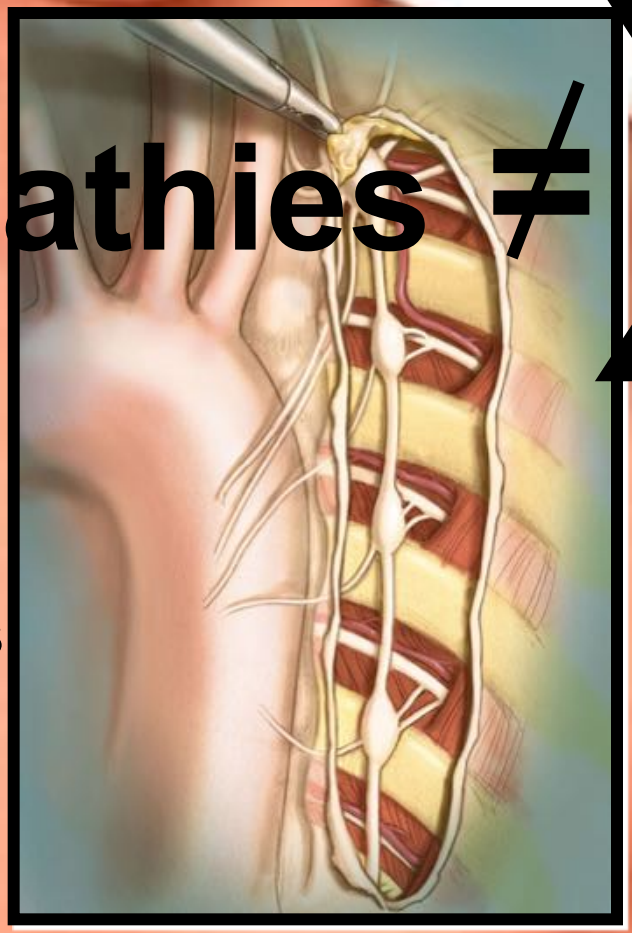
Europace 2013, Heart Rhythm 2013, J of Arrhyth 2013

Primary Prevention ICD: the "In-Between" Groups

Channelopathies ≠ X

Beta-Blocker Therapy
Calcium Channel Blockers
Flecainide
Quinidine



LCSD

FAF

SIDS

SUDS

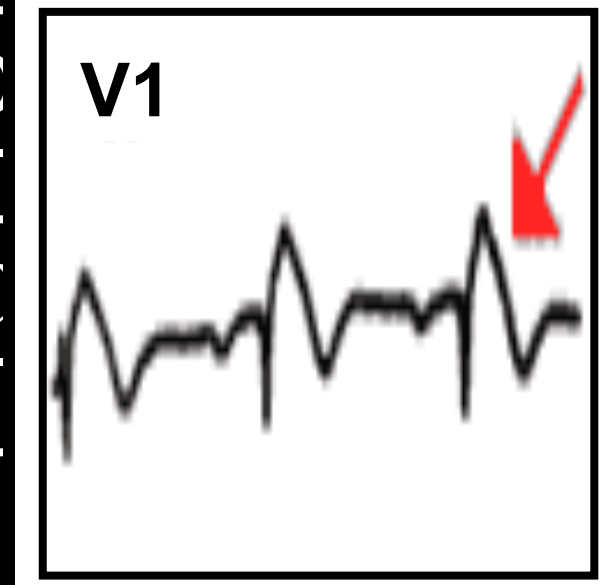
SSS

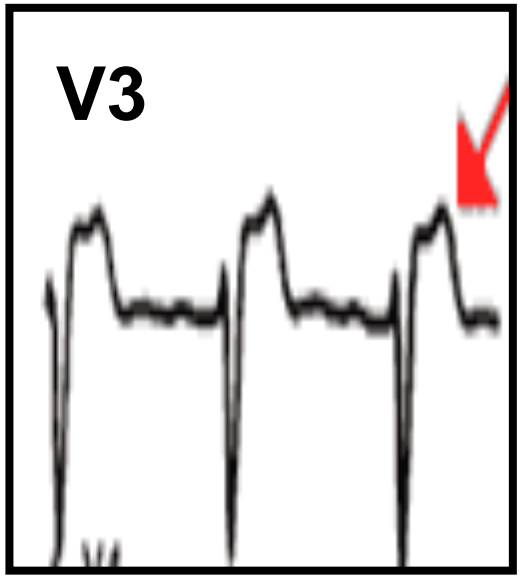
TS

D

C

S





M

S

S

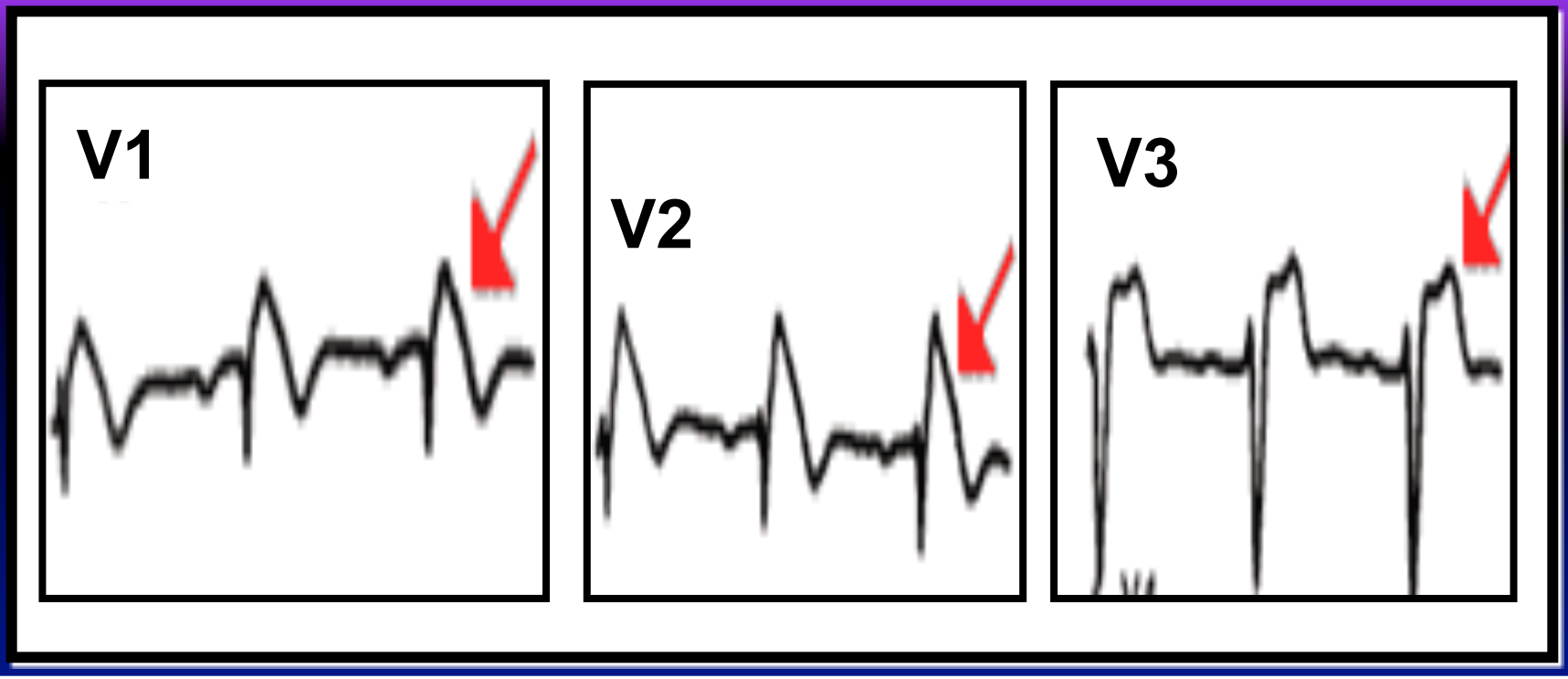
FAVCB

ATS

IVF

BrS

Doyle … MacKinnon. *Science* 280:69-77, 1998



Your patient is a 38-year-old female with this spontaneous ECG. She just fainted in the hot shower. You will recommend a prophylactic ICD.

1. YES
2. NO

Class	ICD Recommendations
Class I	ICD implantation **is recommended** in patients with a diagnosis of BrS who: • Are survivors of a cardiac arrest, and/or • Have documented spontaneous sustained VT with or without syncope.
Class IIa	ICD implantation **can be useful** in patients with a spontaneous diagnostic Type I ECG who have a history of syncope judged to be likely caused by ventricular arrhythmias.
Class IIb	ICD implantation **may be considered** in patients with a diagnosis of BrS who develop VF during programmed electrical stimulation (inducible patients).
Class III	ICD Implantation **is not indicated** in asymptomatic BrS patients with a drug induced type 1 ECG and on the basis of a family history of SCD alone.

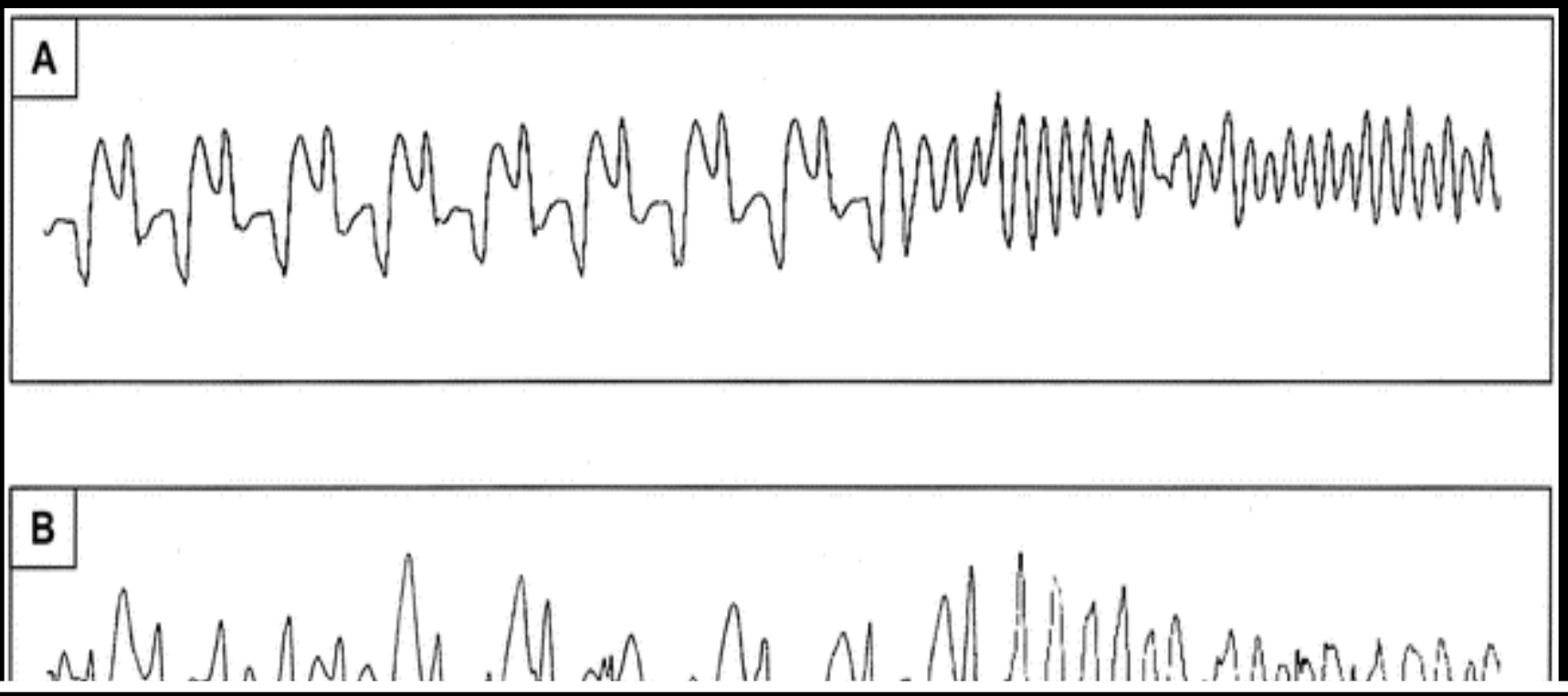
BrS Therapy
Indications for ICD Therapy

?? No BrS Rx Necessary If

- Type 1 Brugada ECG pattern BUT
- Asymptomatic
- EPS – not necessary

  Wilde et al. *JACC* 2010
- PES – 40% inducible but not predictive, 9/14 – Negative

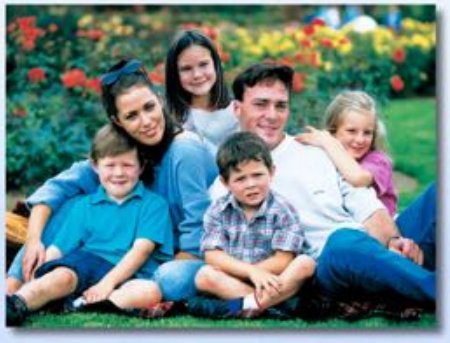
  Priori et al. *JACC* 2012



Your 29-year-old female patient had a near drowning and exercise-induced bidirectional VT (i.e. CPVT). ICD monotherapy is indicated/recommended?

1. YES
2. NO

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)



Clinical

- Exertion Induced Syncope or Sudden Cardiac Death
- No Structural Heart Defect
- Phenotypically Mimics Long QT Syndrome

Exercise-induced PVCs in bigeminy initiating at heart rates > 120 beats per minute – <u>suspicious</u> for CPVT!

Horner … Ackerman. *Heart Rhythm* 2008

Hallmark Arrhythmia

Bi-Directional Ventricular Tachycardia

Expert Consensus Recommendations on CPVT Therapeutic Interventions

Class I	1. The following lifestyle changes ***are recommended*** in all patients with diagnosis of CPVT: a) Limit/ avoid competitive sports; b) Limit/avoid strenuous exercise; c) Limit exposure to stressful environments. 2. Beta-blockers ***are recommended*** in all symptomatic patients with a diagnosis of CPVT. 3. ICD implantation ***is recommended*** in patients with a diagnosis of CPVT who experience cardiac arrest, recurrent syncope or polymorphic/ bidirectional VT despite optimal medical management, and/or LCSD.
Class IIa	4. Flecainide ***can be a useful*** addition to beta- blockers in patients with a diagnosis of CPVT who experience recurrent syncope or polymorphic/ bidirectional VT while on beta-blockers. 5. Beta-blockers ***can be useful*** in carriers of a pathogenic CPVT mutation without clinical manifestations of CPVT (concealed mutation-positive patients).
Class IIb	6. LCSD ***may be considered*** in patients with a diagnosis of CPVT who experience recurrent syncope or polymorphic/bidirectional VT/ several appropriate ICD shocks while on beta-blockers and in patients who are intolerant or with contraindication to beta-blockers.
Class III	7. ICD as a standalone therapy ***is not indicated*** in an asymptomatic patient with a diagnosis of CPVT. 8. Programmed Electrical Stimulation ***is not indicated*** in CPVT patients.

Priori, Wilde, et al. Europace 2013, Heart Rhythm 2013, J of Arrhyth 2013

Indications for ICD Therapy
CPVT-Directed Therapy in CPVT

Emerging Role of Flecainide

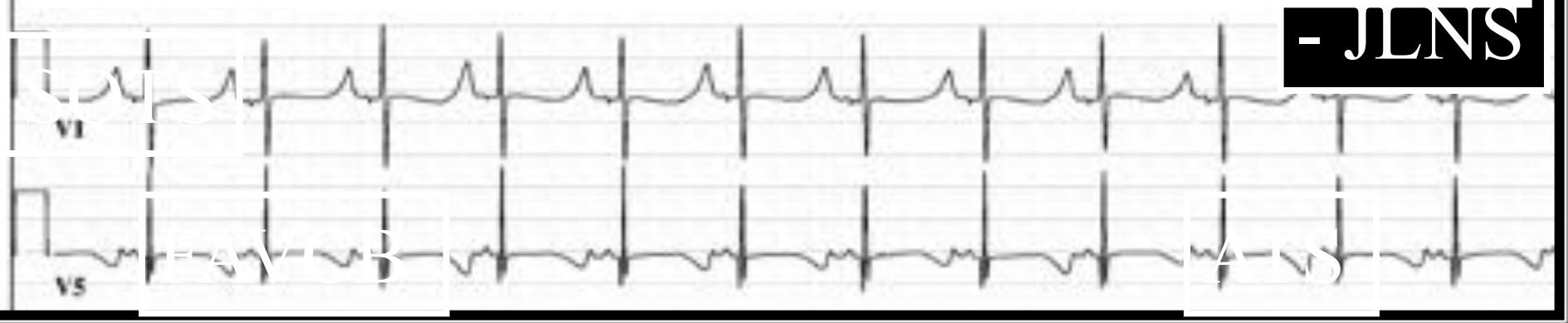
Nadolol/Propranolol Beta Blocker Therapy

- Asymptomatic/CPVT1 Positive

Your 36-year-old female patient fainted while running on a treadmill. Subsequently, you diagnose LQTS and genetically confirm as LQT1.
Her QTc is 503 ms.

You recommend an ICD.

1. YES
2. NO



- JLNS

IVF

BrS

Congenital Long QT Syndrome

Normal QT interval

Prolonged QT

1. Syncope
2. Seizures
3. Sudden death

Torsades de pointes

Long QT Syndrome Recommendations

Class I Recommendations

The following lifestyle changes are recommended in all patients with a diagnosis of LQTS:

- Avoidance of QT prolonging drugs (www.qtdrugs.org)
- Identification and correction of electrolyte abnormalities that may occur during diarrhea, vomiting, metabolic conditions or imbalanced diets for weight loss.

Beta-blockers are recommended for patients with a diagnosis of LQTS who are:

- Asymptomatic with QTc $\geq$ 470 ms, *and/or*
- Symptomatic for syncope or documented VT/VF .

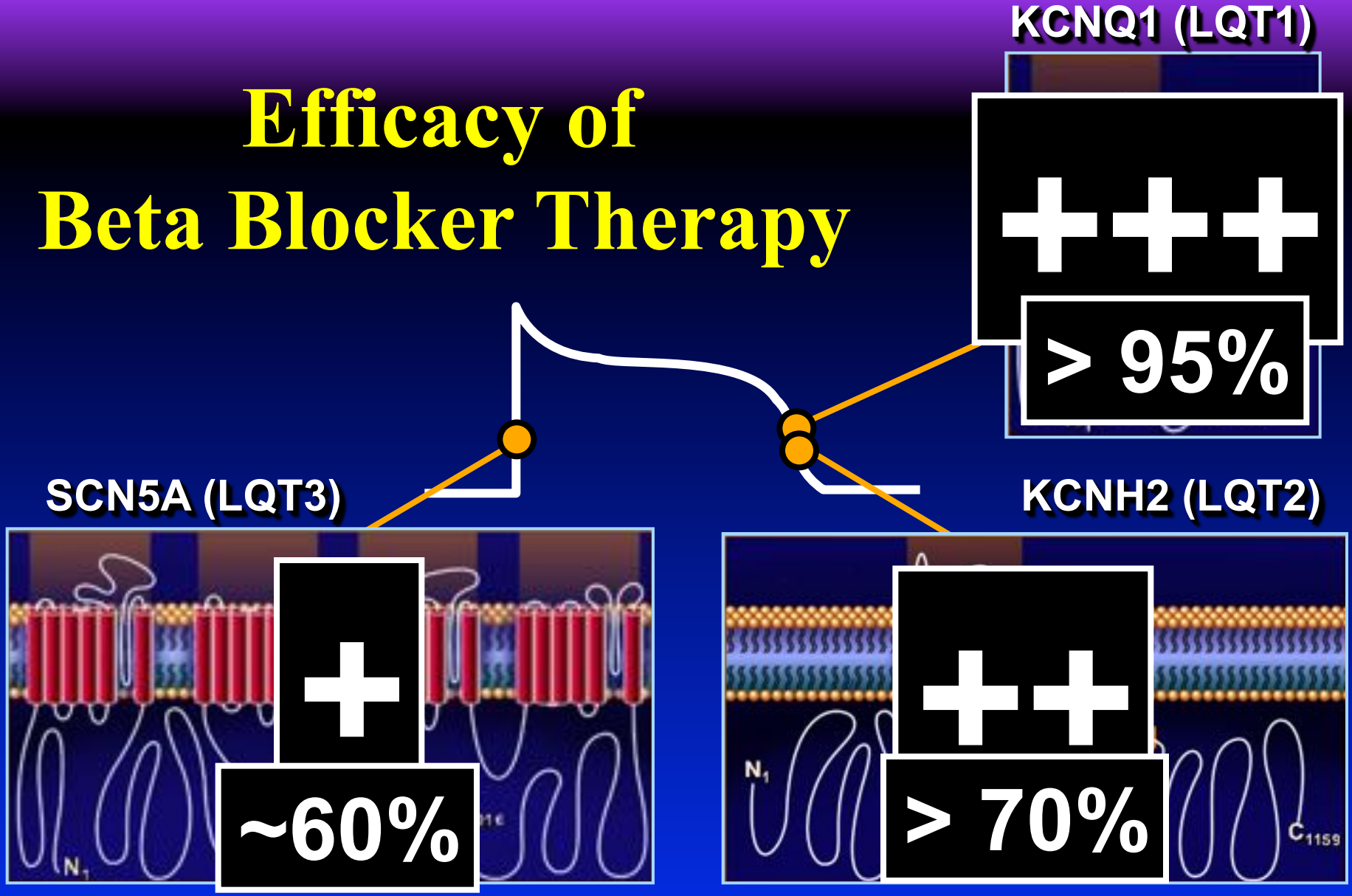
Left cardiac sympathetic denervation (LCSD) is recommended for high-risk patients with a diagnosis of LQTS in whom:

- ICD therapy is contraindicated or refused, *and/or*
- Beta-blockers are either not effective in preventing syncope/ arrhythmias, not tolerated, not accepted or contraindicated.

ICD implantation is recommended for patients with a diagnosis of LQTS who are survivors of a cardiac arrest.

All LQTS patients who wish to engage in competitive sports should be referred to a clinical expert for evaluation of risk.

Efficacy of Beta Blocker Therapy



Moss et al. *Circulation* 101:616-623, 2000
Villain et al. *European Heart Journal* 25:1405-1411, 2004
Ackerman, Priori, Schwartz, Vincent, Wilde. Personal LQTS Clinics, 2015

Long QT Syndrome Recommendations

Class III Recommendation

Except under special circumstances, ICD implantation is **not** indicated in asymptomatic LQTS patients who have not been tried on beta-blocker therapy.

Priori, Wilde, et al. Europace 2013, Heart Rhythm 2013, J of Arrhyth 2013

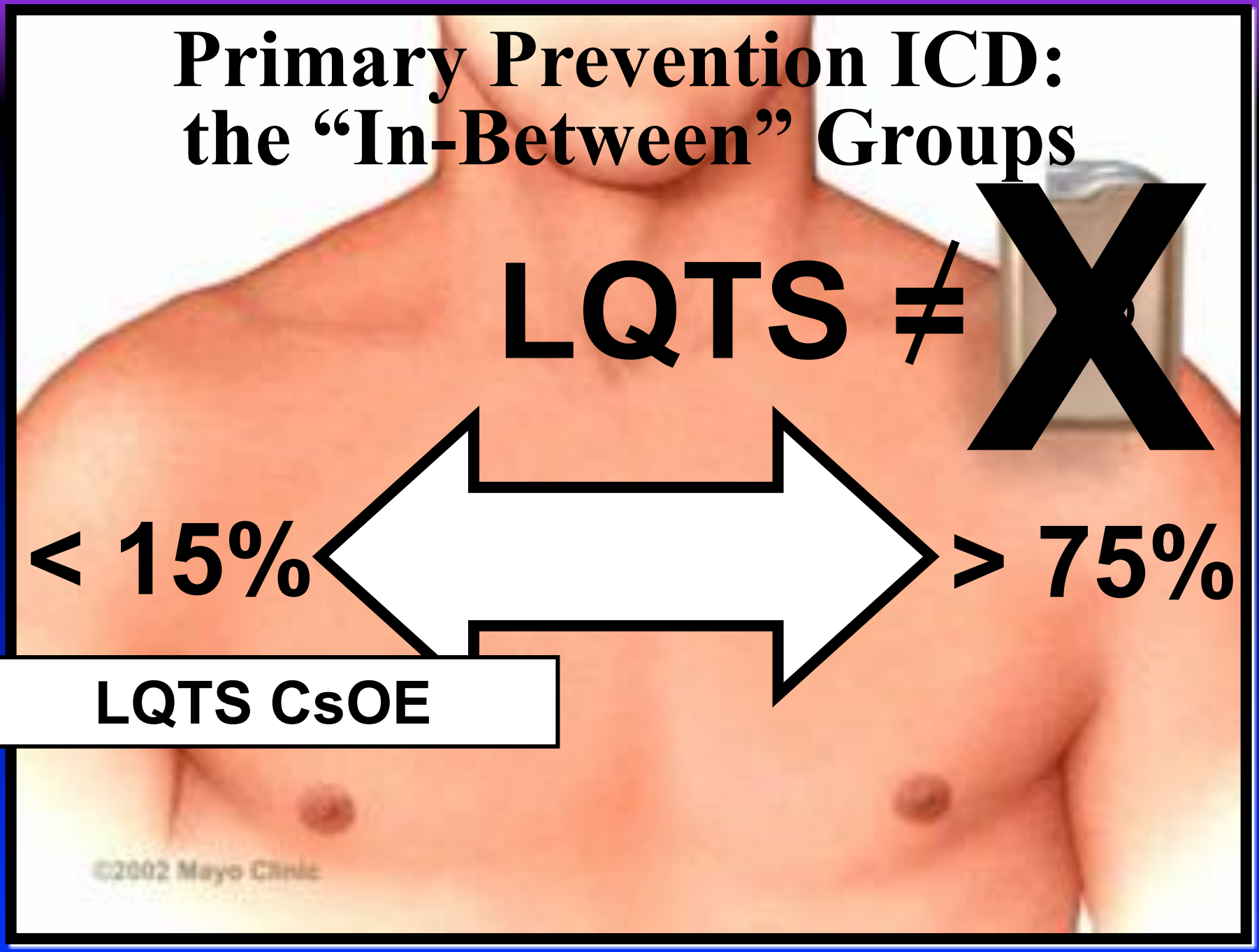
Primary Prevention ICD: the "In-Between" Groups

?? No Active Therapy Necessary If

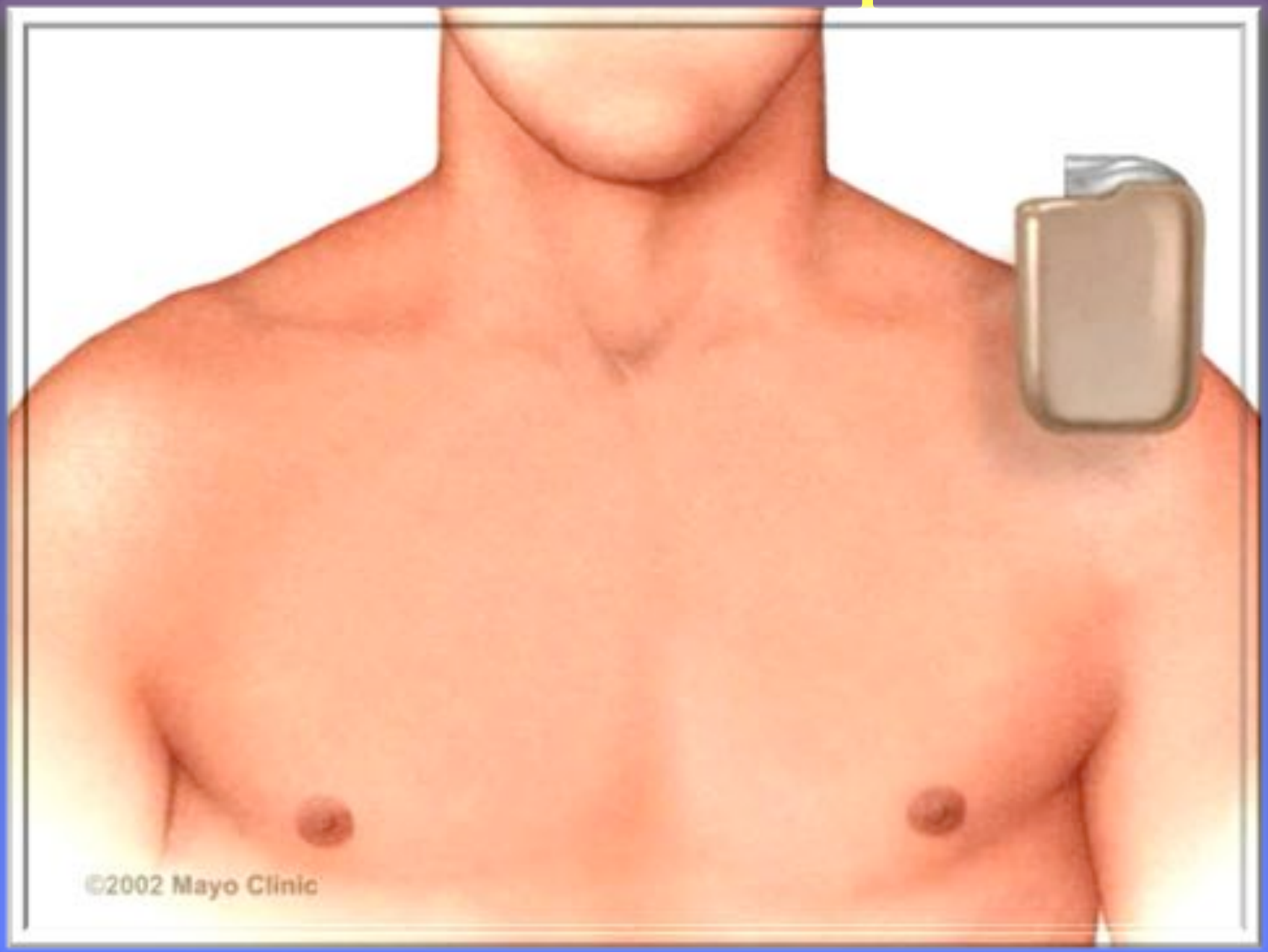
- Asymptomatic male
- > 40 years old
- QTc < 460 ms
- Haploinsufficient, LQT1-causing C-terminal missense mutation

Goldenberg (LQTS Registry). *Circulation* 117:2192-2201, 2008

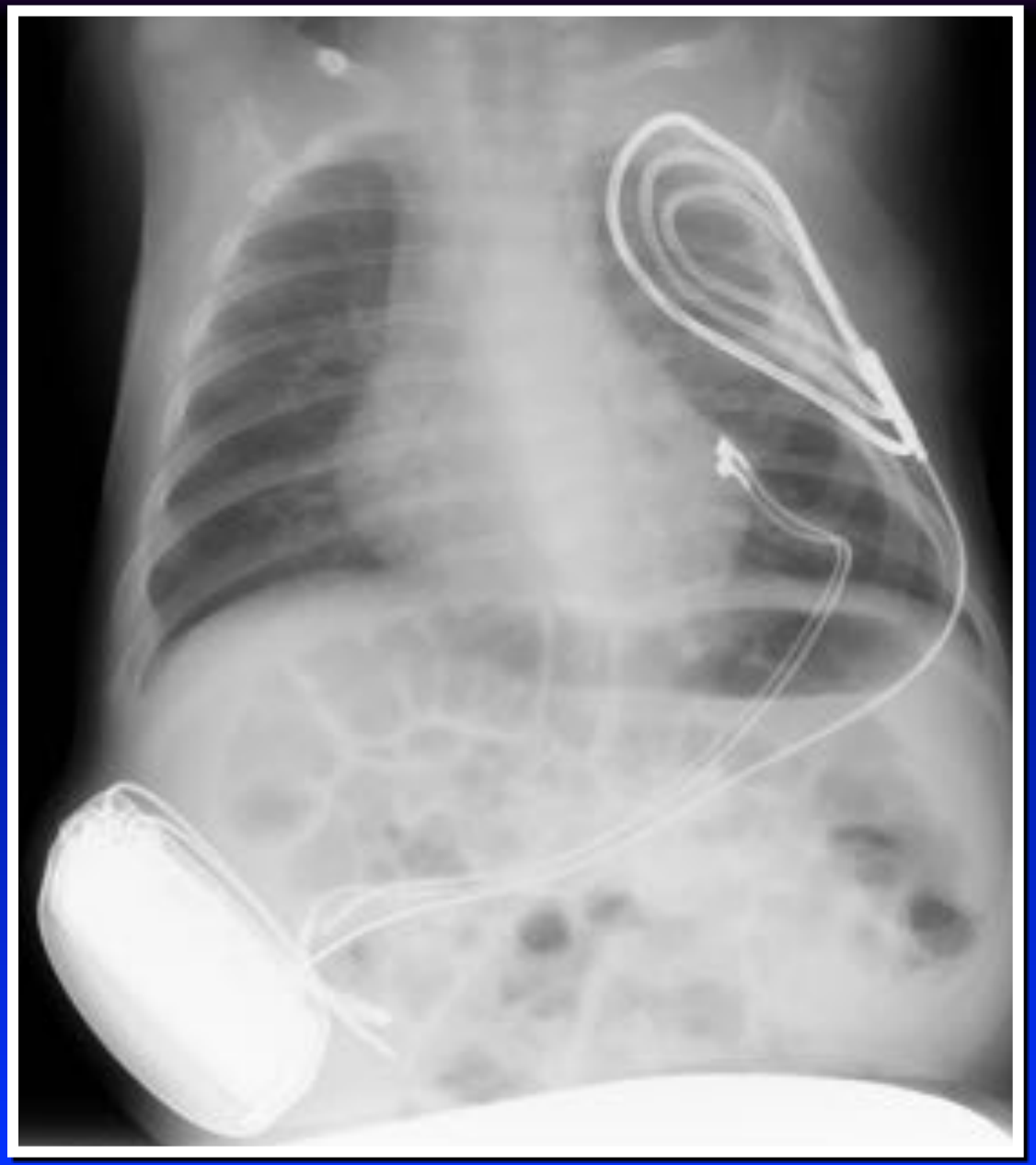
Primary Prevention ICD: the "In-Between" Groups



ICDs and Channelopathies

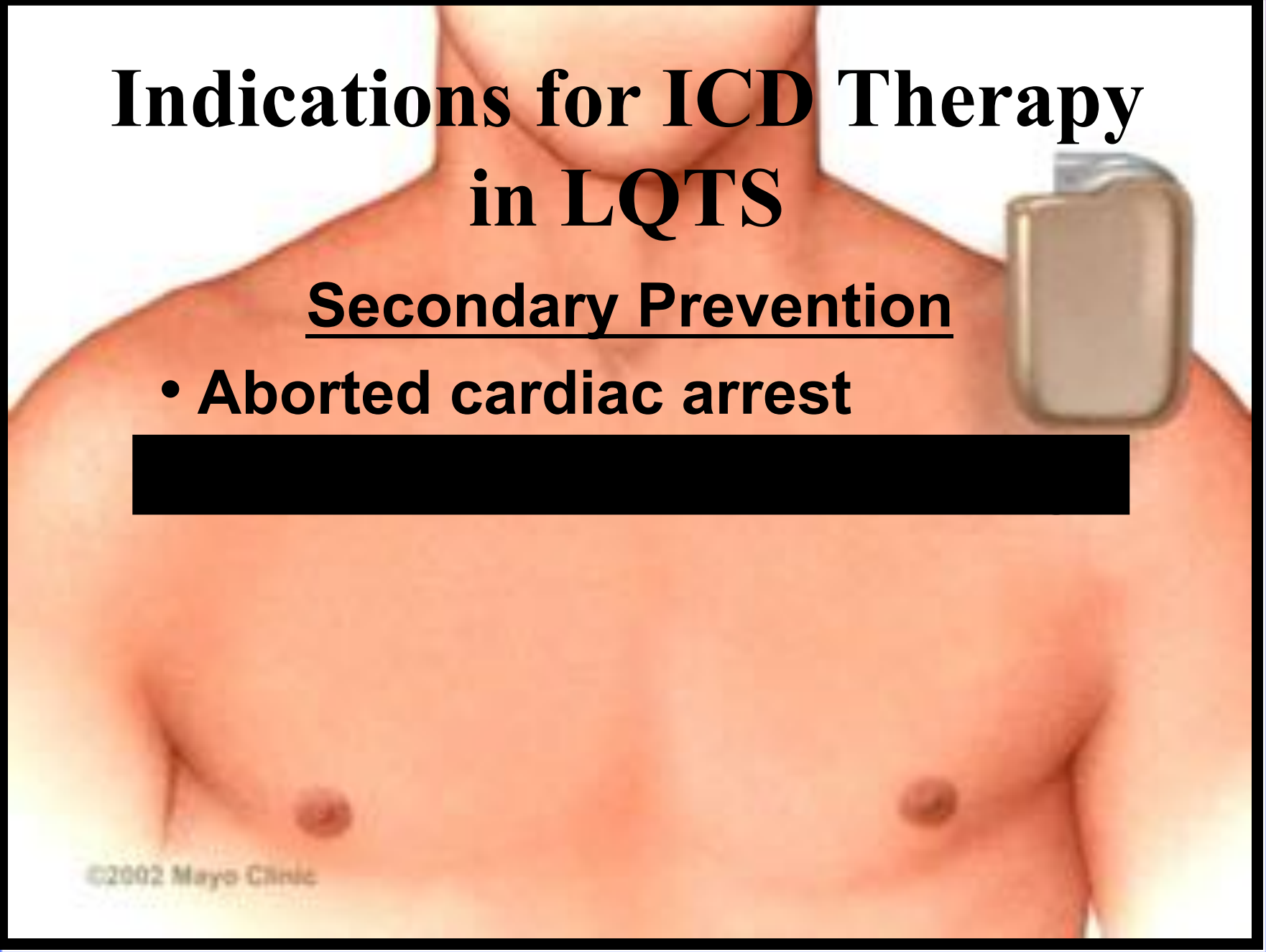


ICDs and Channelopathies



S-ICDs and Channelopathies

Indications for ICD Therapy in LQTS



Secondary Prevention

- Aborted cardiac arrest

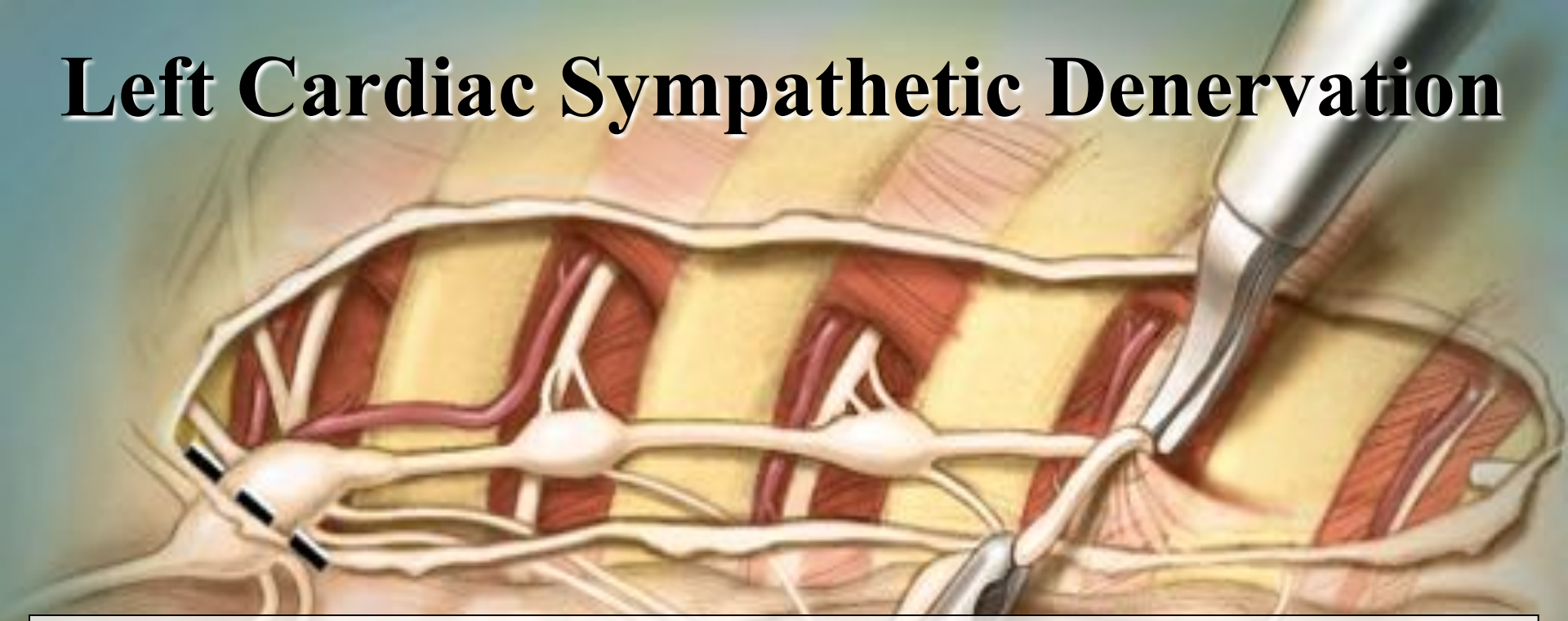
Treatment Options for the Channelopathies

Beta Blocker Rx (LQTS)
Quinidine (BrS)
βBL + Flecainide (CPVT)

LCSD

ICD

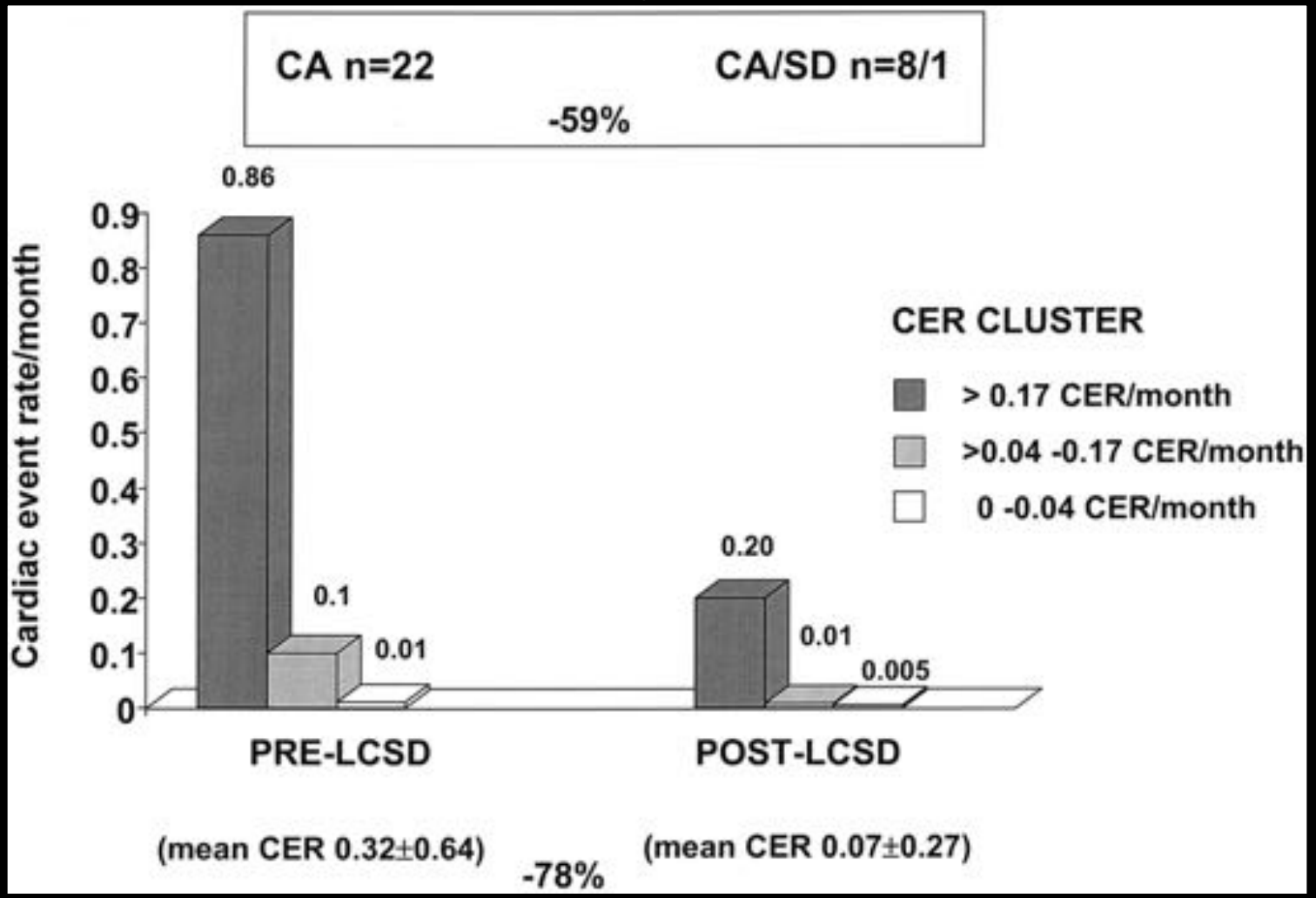
Left Cardiac Sympathetic Denervation



- 1916 - First left stellectomy for angina (Jonnesco)
- 1961 - First bilateral sympathectomy for VT (Estes and Izlar)
- 1968 - First LCSD for VT (Zipes et al.)
- 1970 - First LCSD for LQTS (Moss and McDonald)
- 2003 - First reported videoscopic LCSD for LQTS (Li et al.)
- 2009 - Largest series of videoscopic LCSD (Mayo Clinic)

* **LCSD = Denervation of lower half of the left stellate ganglion (T1) and the sympathetic chain from T2 - T4**

Anti-Fibrillatory Effect of LCSD



Schwartz, P. J. et al. *Circulation* 2004;109:1826-1833

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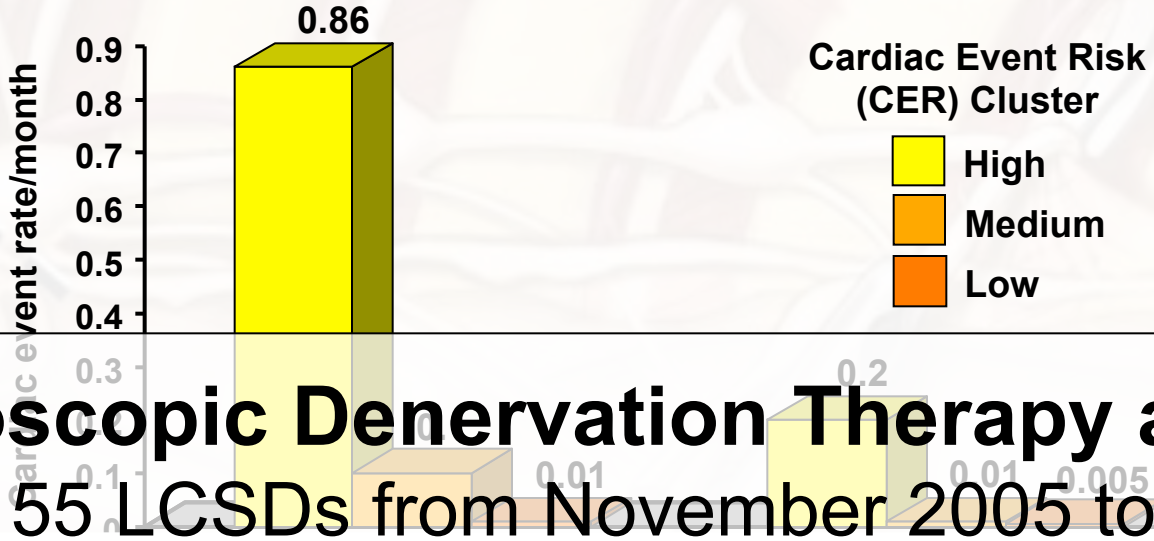
Video-Assisted Thoracic Surgery for Long QT Syndrome

Christopher Moir, M.D.
Michael J. Ackerman, M.D., Ph.D.

Left Cardiac Sympathetic Denervation

- LCSD has a potent anti-fibrillatory effect in LQTS

Schwartz *et al*. Circulation 2004

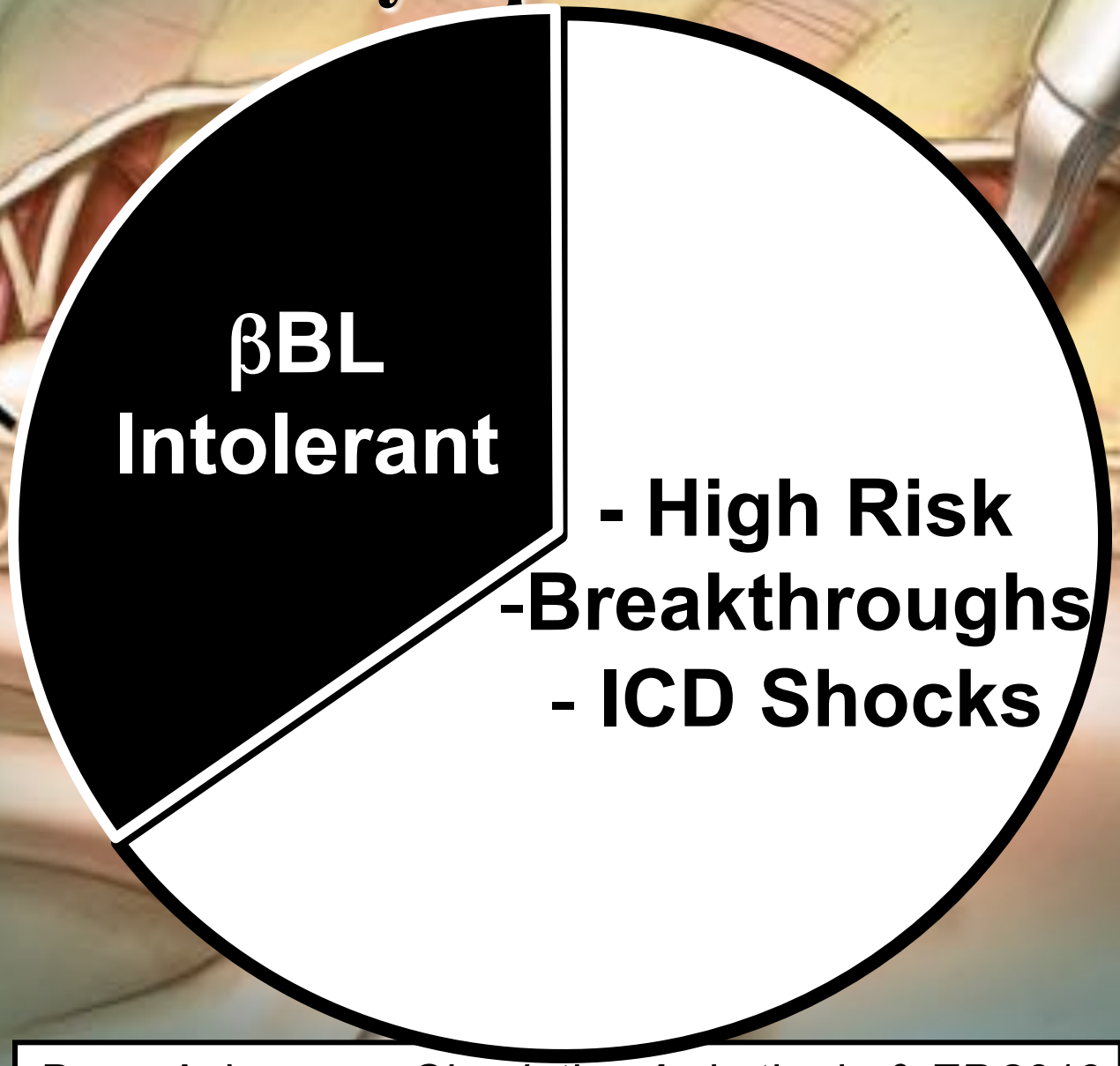


Videoscopic Denervation Therapy at Mayo

- N = 155 LCSDs from November 2005 to present
- Average age: 20 ± 17 years (4 weeks of age to 85 years)
- LQTS (105, LQT1 in 62, LQT2 in 26, LQT3 in 9); CPVT (24); IVF (11); Cardiomyopathy (9)
- LQTS: QTc = 497 ± 67 ms

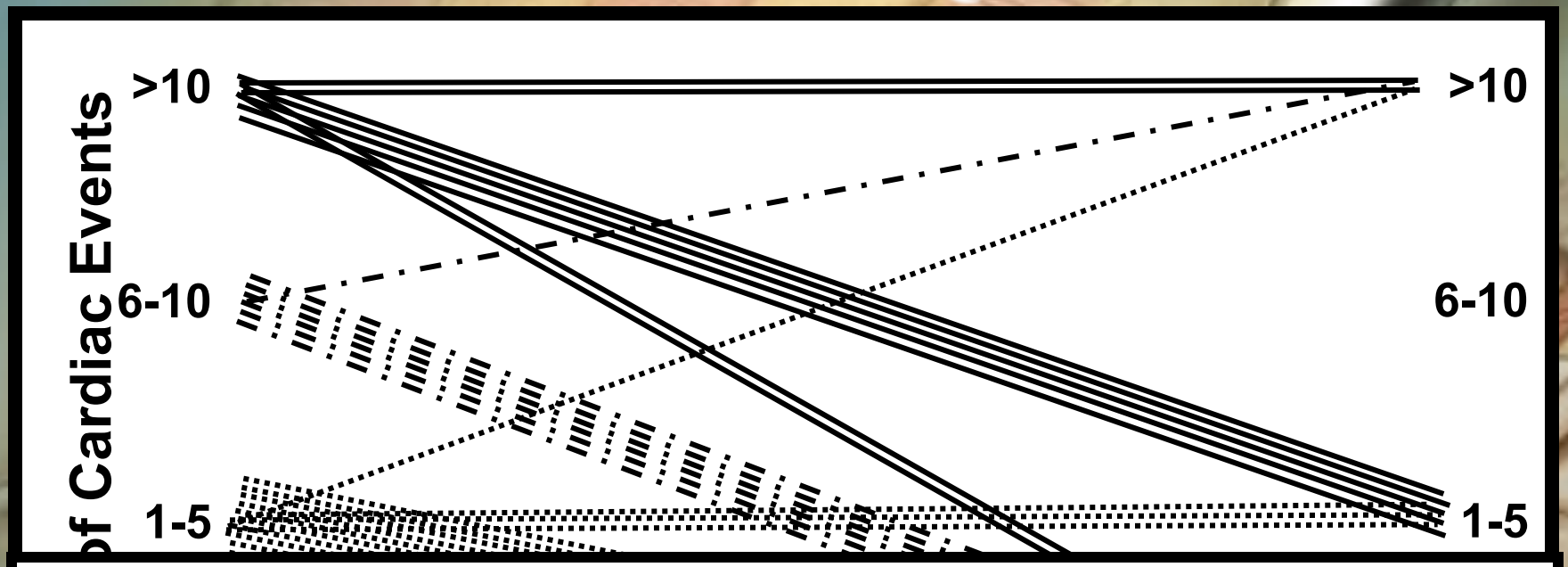
LCSD's anti-fibrillatory effects caused by:
- "Norepinephrine ablation"
- Improved repolarization as evidenced by a decrease in QTc in ~30% ?

Left Cardiac Sympathetic Denervation



Bos…Ackerman. *Circulation Arrhythmia & EP* 2013

LCSD in LQTS



“LCSD is NOT a cure!”

Indications for ICD Therapy in LQTS

Primary Prevention

- QTc > 550 ms and not LQT1
- LQT2 women, QTc > 500 ms, +/- Sx
- Infants with 2:1 AV block?
- JLNS (LQTS w/ deafness)?

Kaufmann (LQTS Registry). *Heart Rhythm* 5:831-836, 2008

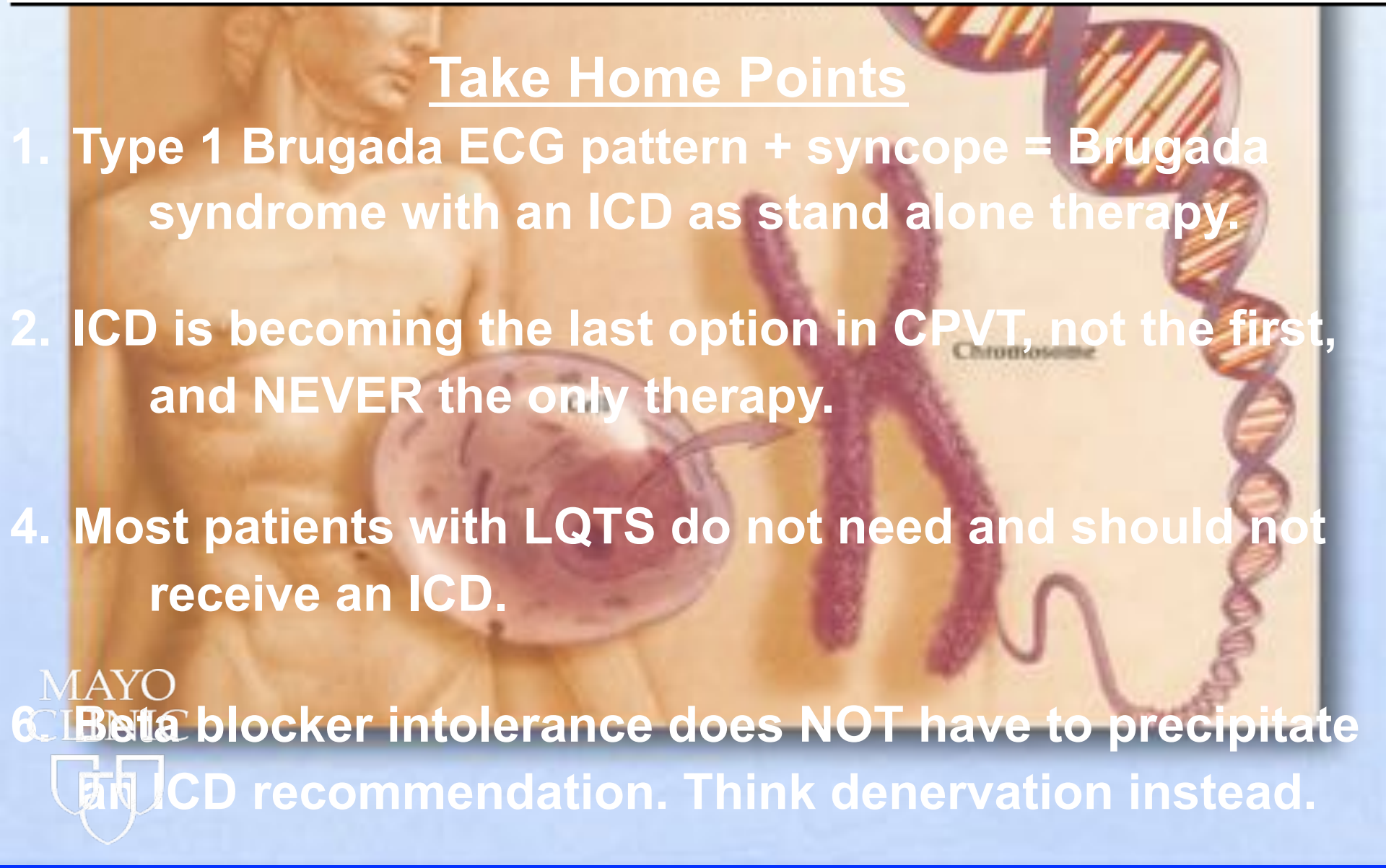
Primary Prevention ICD: the "In-Between" Groups

Beta Blocker Rx (LQTS)
Quinidine (BrS)
βBL + Flecainide (CPVT)

LCSD

ICD

Primary Prevention ICD: The "In-Between" Groups of BrS, CPVT, & LQTS



Take Home Points

1. Type 1 Brugada ECG pattern + syncope = Brugada syndrome with an ICD as stand alone therapy.

2. ICD is becoming the last option in CPVT, not the first, and NEVER the only therapy.

4. Most patients with LQTS do not need and should not receive an ICD.

6. Beta blocker intolerance does NOT have to precipitate an ICD recommendation. Think denervation instead.

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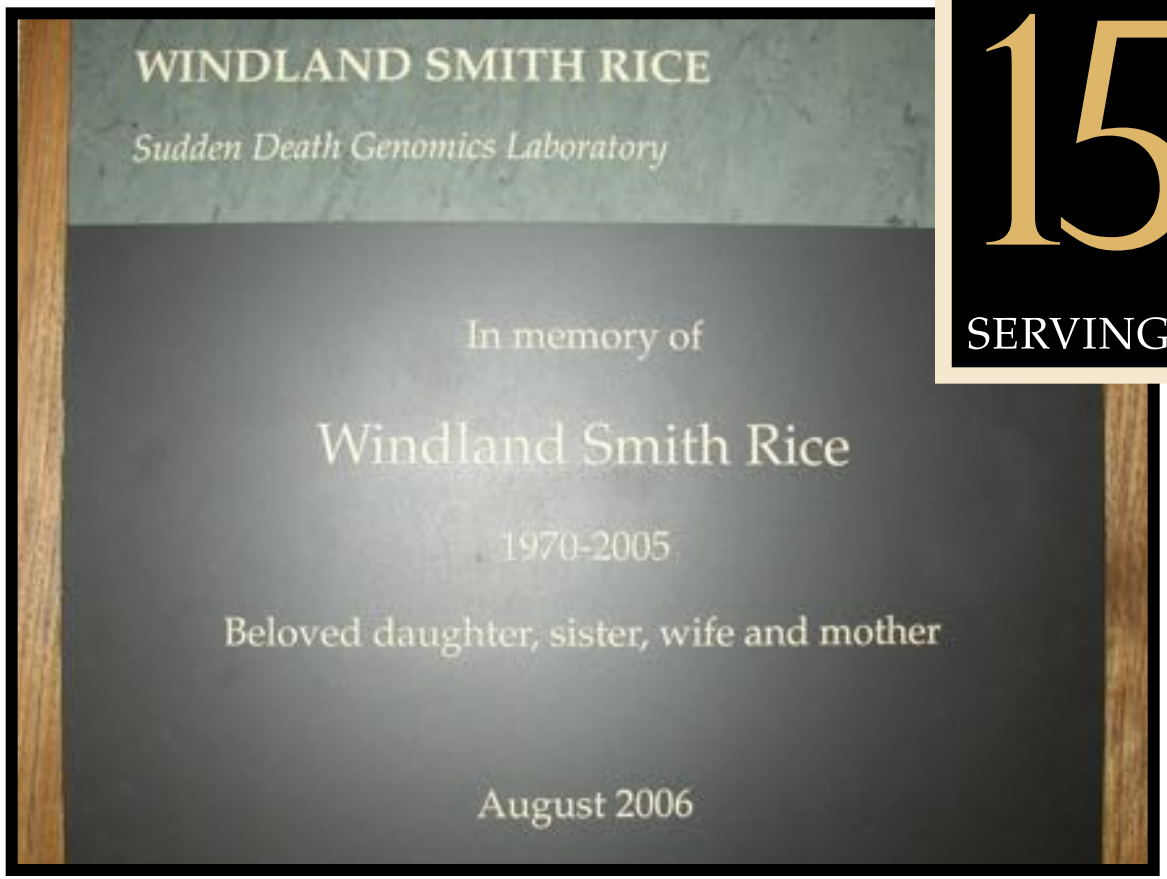

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Dr. Scholl Foundation, CJ Foundation for SIDS

Hannah Wernke Memorial Foundation

Sheikh Zayed Saif Mohammed Al Nahyan Fund

National Institutes of Health

“To heal the sick and advance the science”

Dr. Charles W. Mayo