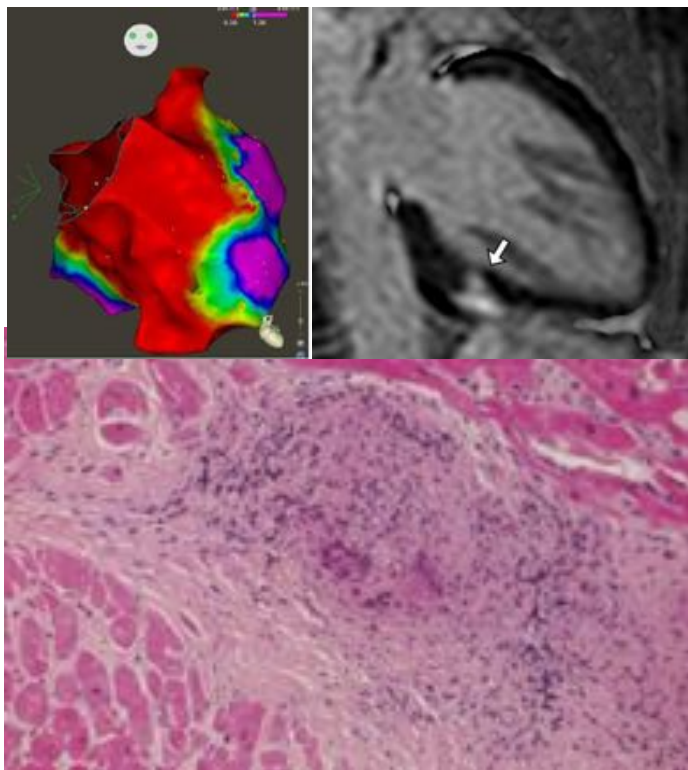




## Primary Prevention ICD: The "In-Between" Groups



# Sarcoid

I Savelieva

St George's University of London, UK

# Cardiac Sarcoidosis

- 1869: skin changes first reported by Jonathan Hutchinson
- 1899: Caesar Boeck described "multiple benign sarkoid of the skin" ("sarcoid of Boeck")
- 1929: myocardial involvement identified by Bernstein
- 1935-39: BBB and CHB in association with sarcoid is reported
- 1952: 20% prevalence of myocardial involvement on autopsy (Longscope and Freiman)
- 1988, 1994: reports of ICD Rx

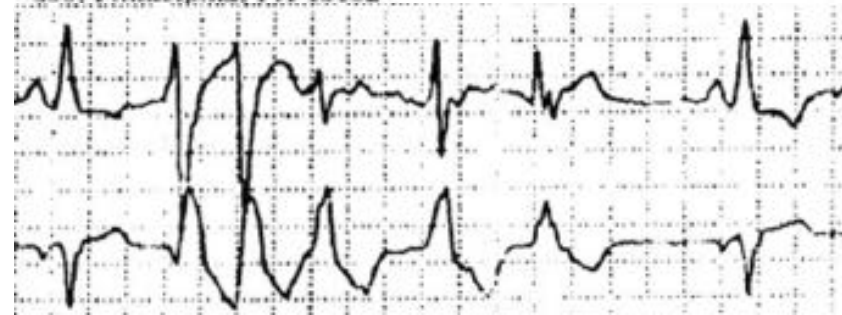
## The Automated Implantable Cardiac Defibrillator\*

CHEST / 106 / 5 / NOVEMBER, 1994

### Prophylaxis in Cardiac Sarcoidosis

*Harold L. Paz, M.D., M.S., F.C.C.P.;*  
*Daniel J. McCormick, D.O.;*  
*Steven P. Kutalek, M.D.;*  
*and Arthur Patchefsky, M.D.*

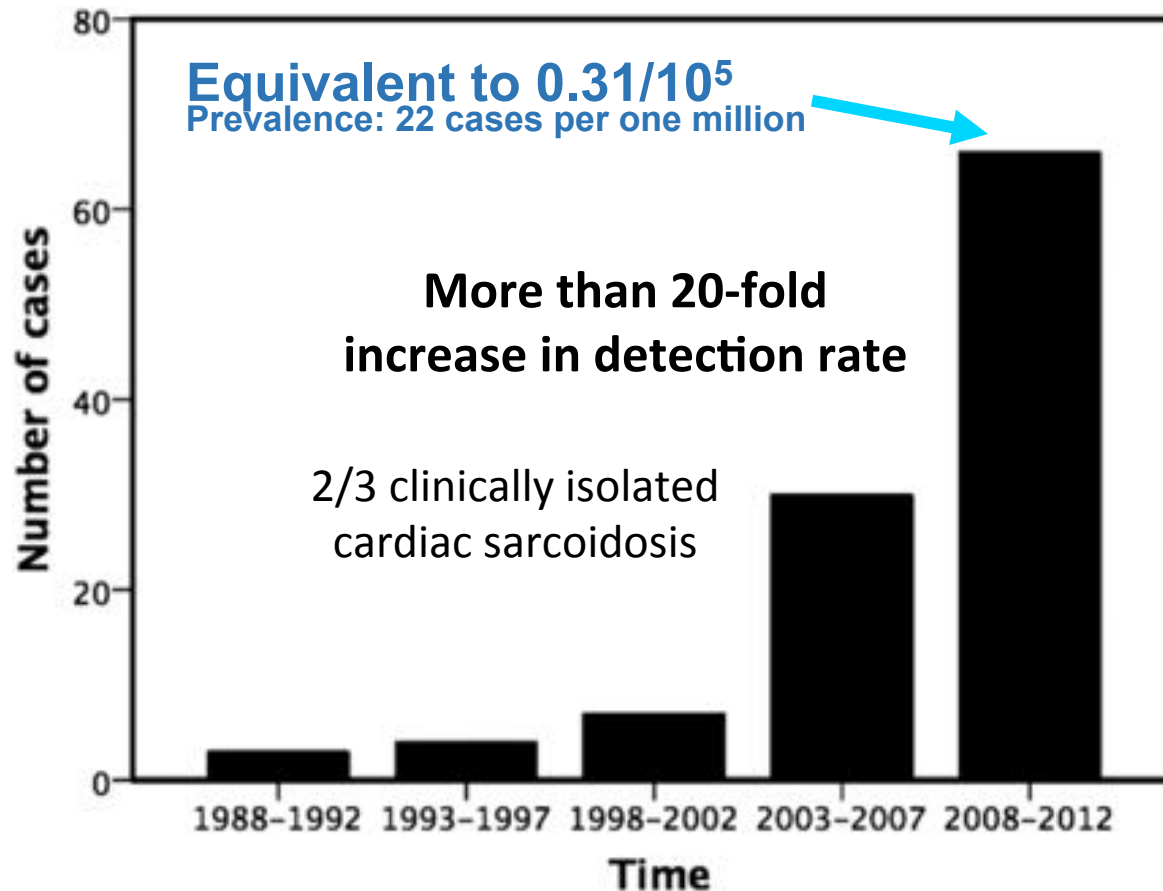
\*From the Divisions of Allergy, Critical Care, Pulmonary Medicine, and Cardiology, Department of Medicine, and Department of Pathology, Hahnemann University, Philadelphia.  
Reprint requests: Dr. Paz, Hahnemann University, Mail Stop 300, Philadelphia, PA 19102



# Prevalence of Sarcoidosis

- Prevalence world-wide: 4.7 - 64 per 100,000
- Scandinavia: 50-60 per 100,000
- U.S.: 10.9 per 100,000 in whites,  
35.5 per 100,000 in African Americans
- 25-39% cardiac involvement (mortality 13-25%)
- Common cardiac involvement (58%) in Japan  
(mortality 85%)

# Epidemiology of Cardiac Sarcoidosis: 25-year Nationwide Study



The number of new cases of cardiac sarcoidosis in Finland diagnosed in 5-year periods between 1988 and 2012

# Epidemiology of Cardiac Sarcoidosis: 25-year Nationwide Study

Survival Probabilities in All 110 CS Patients and in the 102 Patients Diagnosed Before Transplantation or Autopsy

|                  | Cardiac Survival, n | Cardiac Survival Free of Transplantation | Cardiac Survival Free of Transplantation and Aborted Sudden Death | Cardiac Survival |            |
|------------------|---------------------|--|---|------------------|------------|
| 1- y survival, % | 110                 | 99.1 (94.3–99.9)                         | 97.3 (91.6–99.3)  | 89.1 (81.3–93.9) | <b>3%</b>  |
|                  | 102                 | 100 (95.5–100)                           | 99.0 (93.9–99.9)  | 89.2 (81.1–94.2) |            |
| 5-y survival, %  | 110                 | 93.5 (86.7–97.1)                         | 90.0 (82.4–94.6)  | 77.7 (68.5–84.8) | <b>10%</b> |
|                  | 102                 | 97.0 (90.9–99.2)                         | 95.1 (88.4–98.2)  | 82.0 (72.9–88.7) |            |
| 10-y survival, % | 110                 | 89.3 (81.6–94.2)                         | 83.1 (74.5–89.3)  | 70.4 (60.8–78.5) | <b>17%</b> |
|                  | 102                 | 92.5 (85.1–96.5)                         | 90.6 (82.7–95.2)  | 77.2 (67.6–84.7) |            |

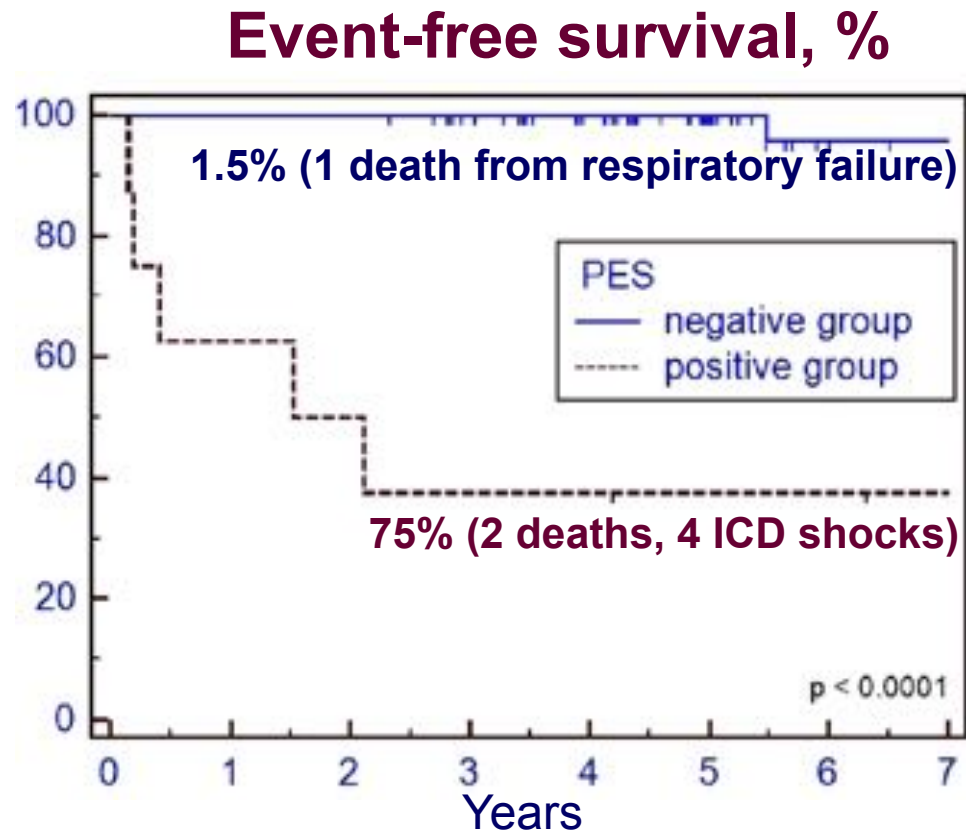
More favorable mortality than previously reported - ? due to earlier diagnosis  
Heart failure at presentation predicted poor outcome (log-rank  $P=0.0001$ ) with a  
10-year transplantation-free cardiac survival of only 53%

# EP Effects of Cardiac Sarcoidosis

| EP effect                    | Prevalence |
|------------------------------|------------|
| AV block                     | 26-62%     |
| Bundle branch block          | 12-61%     |
| Complete heart block         | 22-30%     |
| Ventricular tachycardia      | 23-50%     |
| Sudden death                 | 12-65%     |
| Supraventricular tachycardia | 19-32%     |

# Role of Electrophysiological Study in Risk Stratification

- N = 76, age ~49 years
- Sarcoidosis confirmed by biopsy
- CS confirmed on PET or MRI
- Inducible VT: n = 8 (10.5%)
- Pts with VT received ICD
- EF < 40% inducible VT vs non-inducible VT: 62.5% vs 26.5%
- Corticosteroid Rx: 61-71%
- Endpoint: survival and arrhythmic events
- Follow-up: 5 years



**PES may help to guide ICD use in CS**



## 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Electrophysiological study may be considered for the differential diagnosis of ARVC and benign RVOT tachycardia or sarcoidosis.

**IIb**

**B**



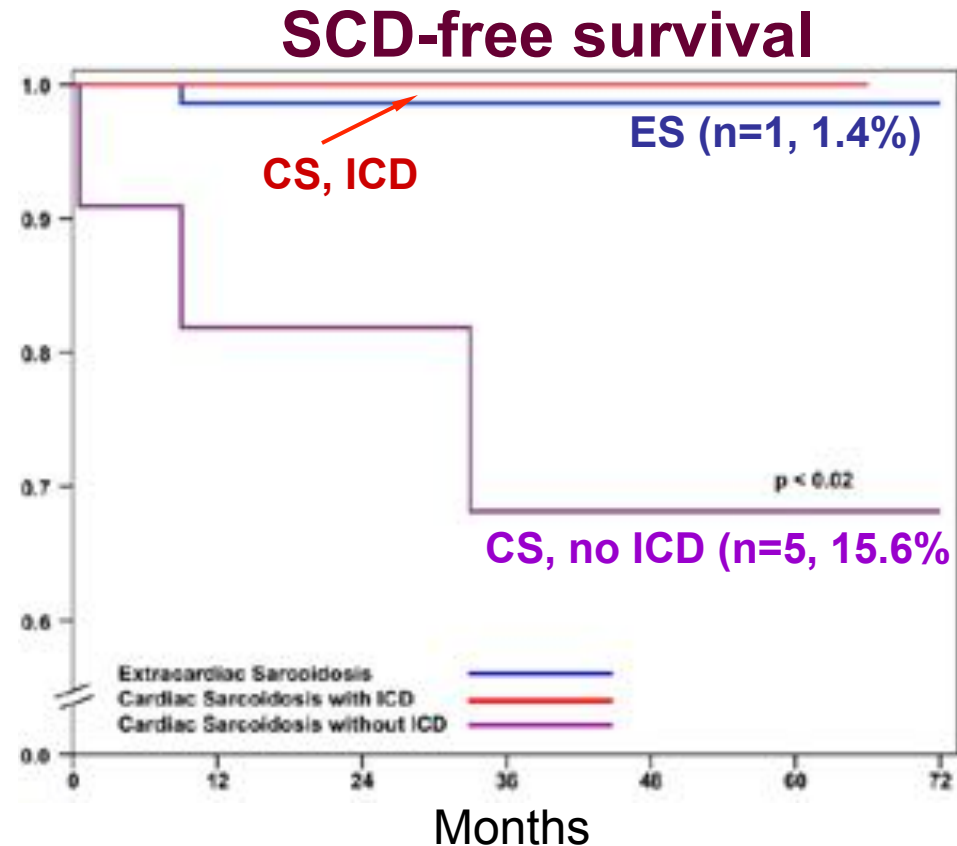
# HRS Expert Consensus Statement on Diagnosis and Management of CS: Tools for Risk Stratification

| Recommendation   | Class |
|--|-------|
| <b>Assessment of myocardial inflammation with FDG-PET can be useful in CS patients with ventricular arrhythmias</b>  | IIa   |
| <b>An EP study for the purpose of sudden death risk stratification may be considered in patients with LVEF &gt; 35%, despite OMT and a period of immunosuppression (if there is active inflammation)</b> | IIb   |
| <b>CMR for the purpose of sudden death risk stratification may be considered in patients with CS</b>   | IIb   |

The writing group agreed, however, that data from the major primary and secondary prevention ICD trials were relevant. Hence, it follows that the recommendations from the general device guideline documents apply to this population.

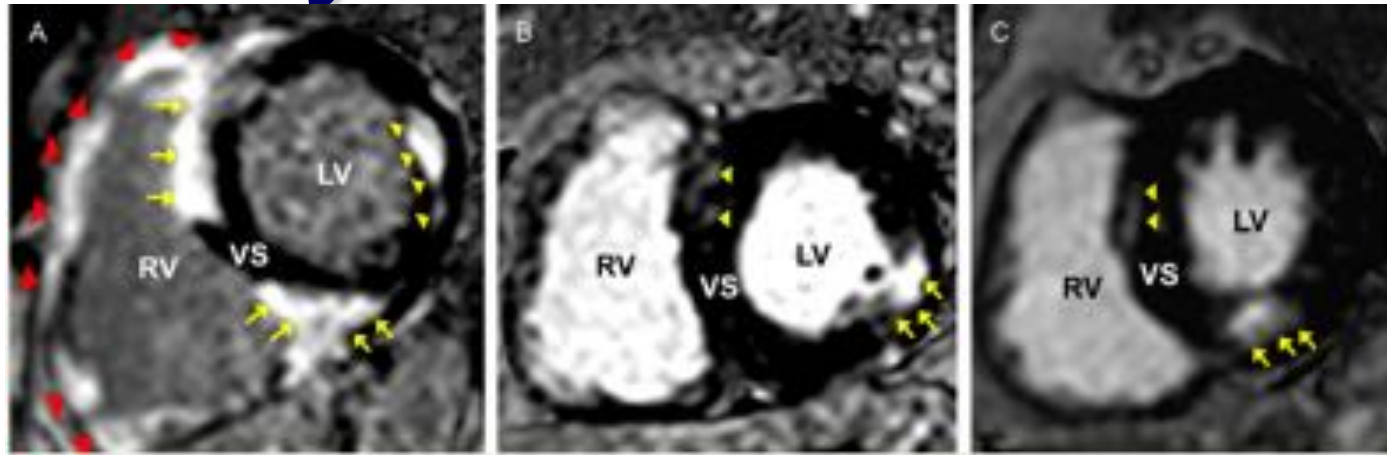
# Role of LGE-MRI in Risk Stratification

- Single-centre study, Melbourne
- N = 106, age ~51 years, 60% men
- Sarcoidosis confirmed by biopsy
- Immunosuppressive Rx: 57.5%)
- 1° EP: composite of SCD, VT, VF
- 2° EP: ACM
- Follow-up: 2.5 years
- **CS on MRI: n = 32 (30%)**



**Risk of SCD was 11-fold higher in CS  
ICD was protective**

# Predictive Value of DE on MRI in Primary Prevention Patients



| DE pattern    | Sens., % | Spec., % | PPV, % | NPV,% |
|---------------|----------|----------|--------|-------|
| Any DE        | 100      | 69       | 22     | 100   |
| RV DE         | 67       | 100      | 100    | 97    |
| LV DE         | 100      | 69       | 22     | 100   |
| Multifocal DE | 67       | 94       | 48     | 97    |

# Treatment Options for Arrhythmias in Cardiac Sarcoidosis

- **Immunosuppression**
- **Antiarrhythmic drugs**  
**(amiodarone, sotalol)**
- **Catheter ablation**
- **ICD**

**ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: A Report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): Developed in Collaboration With the European Heart Rhythm Association and the Heart Rhythm Society**

## **8.4.2. Infiltrative Cardiomyopathies**

### Recommendations

#### **Class I**

In addition to managing the underlying infiltrative cardiomyopathy, life-threatening arrhythmias should be treated in the same manner that such arrhythmias are treated in patients with other cardiomyopathies, including the use of ICD and pacemakers in patients who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)



## 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

ICD implantation may be considered earlier in patients with giant cell myocarditis or sarcoidosis who had haemodynamically compromising sustained VA or aborted cardiac arrest, due to adverse prognosis of these conditions, if survival  $>1$  year with good functional status can be expected.

**IIb**

**C**

# ICD for Prevention of SCD in SC

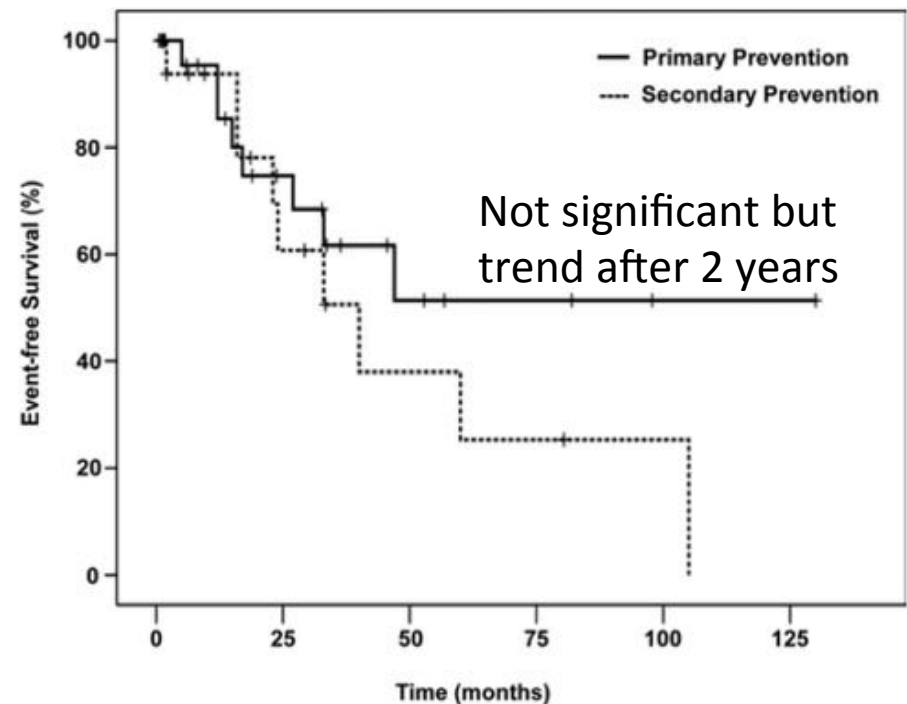
| Study          | Design              | N   | 1° prevention | F-UP, years | App propr. Rx/year | AEs   |
|----------------|---------------------|-----|---------------|-------------|--------------------|-------|
| Kron, 2013     | U.S., Canada, India | 235 | 62.6%         | 4.2±4.0     | 8.6%               | 17.4% |
| Betensky, 2012 | U.S.                | 45  | 64.4%         | 2.6±2.7     | 14.5%              | 15.6% |
| Schuller, 2012 | U.S.                | 112 | 74.1%         | 2.8         | 13.2%              | -     |

# Cardiac Sarcoidosis: Long-term Follow-up and ICD Therapy

45 pts with ICDs, biopsy-proven systemic sarcoidosis, and cardiac involvement (histopathology, MRI, and/or PET)

Device logs and medical records were retrospectively reviewed

Appropriate ICD therapies for VT/VF  
37.8% of the patients (15% per year)  
Inappropriate ICD therapies 13.3%



**Longer ICD follow-up (4.5 3.1 years vs 1.5 1.5 years;  $P$  .001), depressed LVEF (35.5% 15.5% vs 50.9% 15.5%;  $P$  .002), and CHB (47.1% vs 17.9%;  $P$  .048) associated with appropriate ICD therapy**



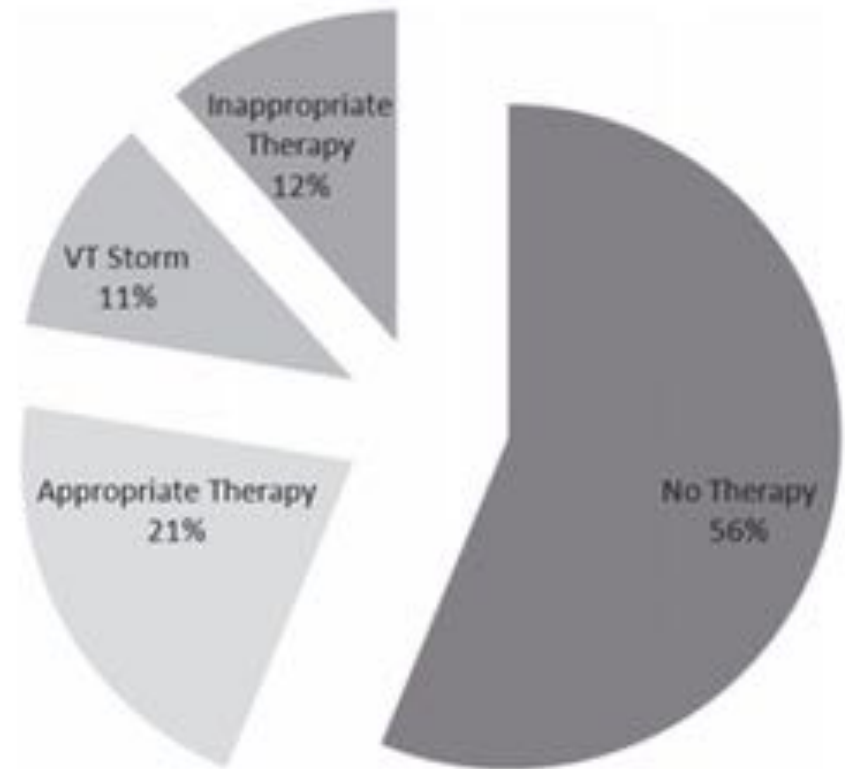
# Cardiac Sarcoidosis: ICD Therapy

112 patients with cardiac sarcoidosis (biopsy proven) and an ICD implanted for primary or secondary prevention

Mean follow-up 29 months

Covariates associated with appropriate ICD therapies included:

- Left ventricular ejection fraction (LVEF) <55% (OR 6.52 [95% CI 2.43–17.5])
- Right ventricular dysfunction (OR 6.73 [95% CI 2.69–16.8])
- Symptomatic heart failure (OR 4.33 [95% CI 1.86–10.1])



# HRS Expert Consensus Statement on Diagnosis and Management of CS: Indications for ICD

| Recommendation   | Class |
|--|-------|
| LVEF $\leq$ 35%, despite OMT and a period of immunosuppression (if active inflammation is present)                                 | I     |
| An indication for permanent pacemaker exists   | IIa   |
| Unexplained syncope or near-syncope, believed to be arrhythmic in origin   | IIa   |
| Inducible sustained ventricular arrhythmias or clinically relevant VF  | IIa   |
| LVEF range 36-49% and or an RVEF $<$ 40%, despite OMT for CHF and a prior of immunosuppression (if active inflammation is present) | IIb   |

# HRS Expert Consensus Statement on Diagnosis and Management of CS: Indications for ICD

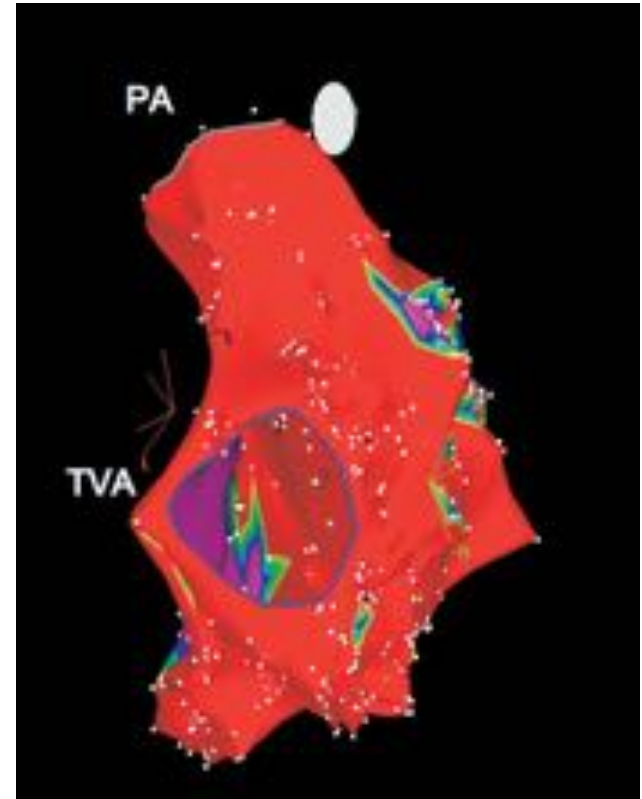
| <b>Recommendation</b>  | <b>Class</b> |
|--|--------------|
| No history of syncope, normal LVEF/RVEF, no late gadolinium enhancement on CMR, negative EP study, and no indication for permanent pacemaker | III          |
| Severe NYHA class IV heart failure   | III          |
| Incessant ventricular arrhythmias  | III          |

# VT Ablation in Cardiac Sarcoidosis

| Study           | M | EF,% | Non-inducible post | Partial success | Recurrence | Follow-up, mos |
|-----------------|---|------|--------------------|-----------------|------------|----------------|
| Koplan, 2006    | 8 | 34   | 2/8 (25%)          | 4/9             | 6/8 (75%)  | 6-84           |
| Jefic, 2009     | 9 | 42   | 5/9 (56%)          | 3/9             | 4/9 (44%)  | 19.8           |
| Dechering, 2013 | 8 | 36   | 5/8 (63%)          | -               | -          | 6              |

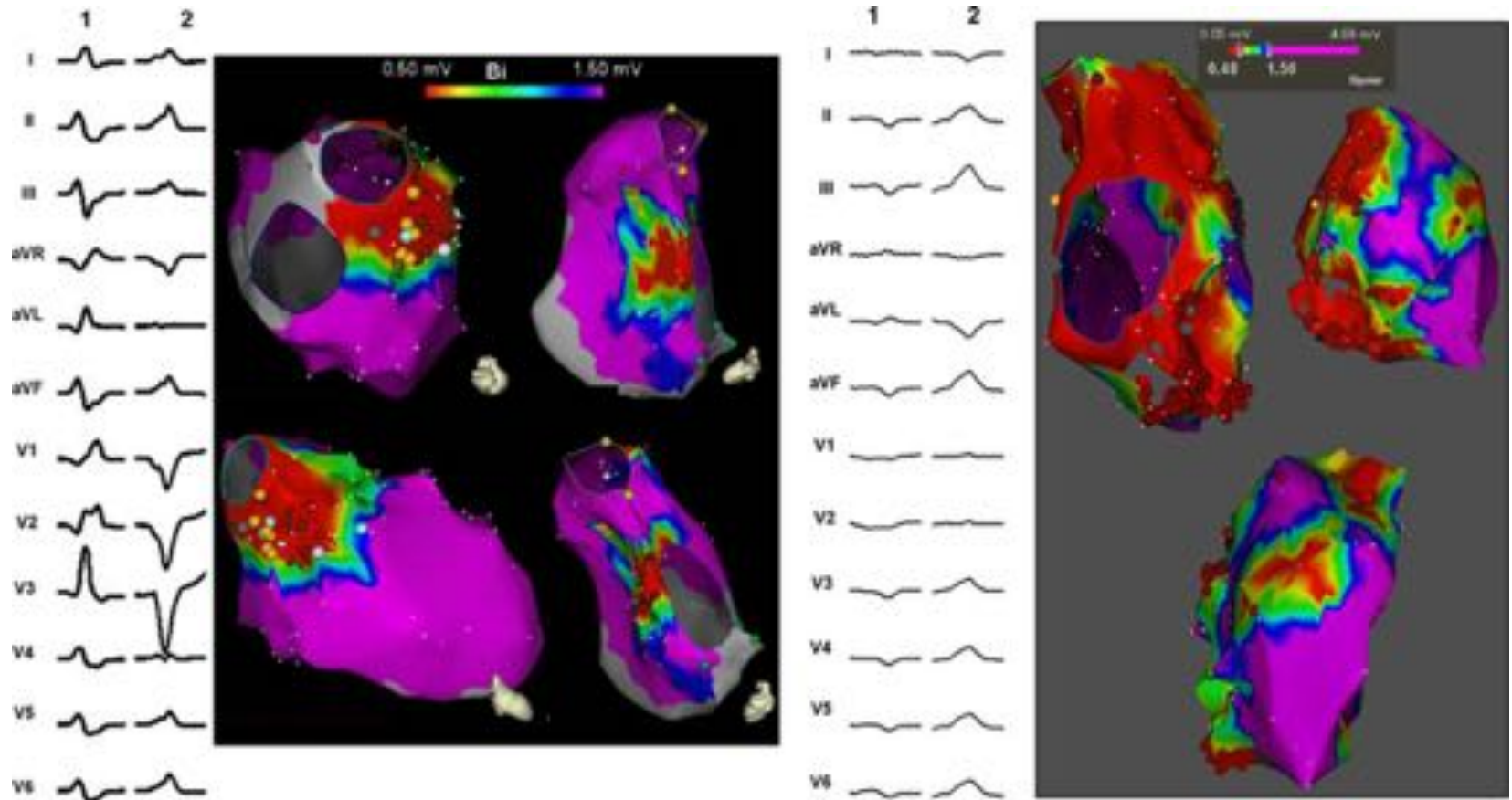
# Cardiac Sarcoidosis and RF Ablation

- Radiofrequency ablation in 9 patients (age 46.7 years, LVEF 42%) with VT not controlled by medical therapy
- Total of 44 VTs (mean CL 348 ms) were induced
- Endocardial RFA performed in 8 pts (RV 5, LV 3) and epicardial RFA in 1 patient.
- Elimination of 31 (70%) of 44 VTs
- **Most frequent VT circuit was reentry in the peritricuspid area**
- Arrhythmic events decreased from  $271 \pm 363$  episodes pre-ablation to  $4.0 \pm 9.7$  post-ablation. Decrease (n=4) or complete elimination (n=5) of VT during mean follow-up of 19.8 months



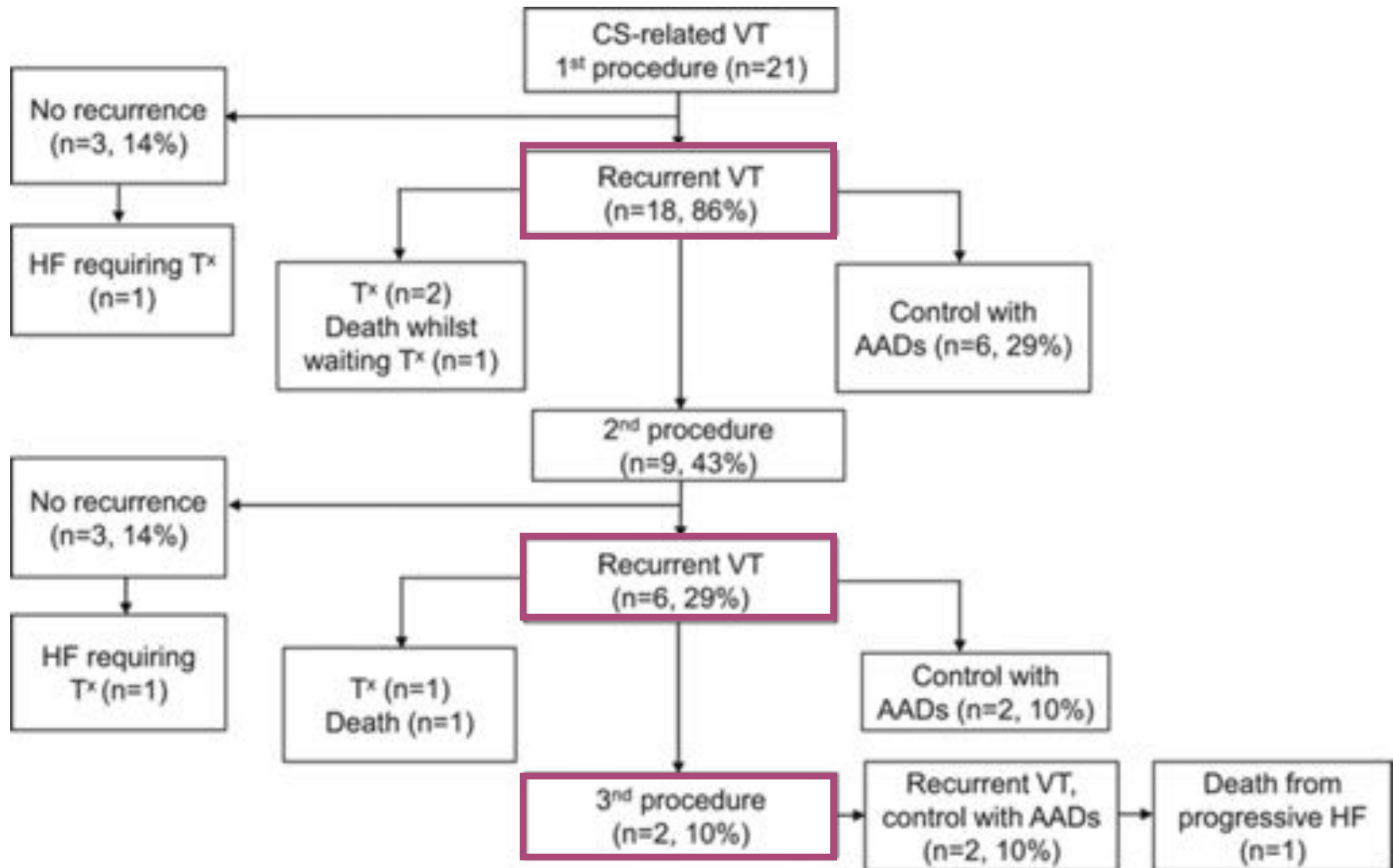
Low voltage bipolar electrograms (<1.5 mV) around the tricuspid annulus

# Multiple VTs in Cardiac Sarcoidosis



*Kumar et al. Circ Arrhythm Electrophysiol 2015;8:87-93*

# Outcomes after catheter ablation



# Conclusions

- Cardiac sarcoidosis is a relatively rare condition which has recently been diagnosed more frequently because of a wider use of modern imaging modalities
- Ventricular tachyarrhythmias and sudden death occur frequently
- EP study and MRI are helpful in risk stratification in addition to presentation with HF
- Treatment consists of immunosuppression, AADs, and non-pharmacological therapies
- ICD placement is encouraged early after the occurrence of VTAs
- Primary ICD prevents SCD, but data are limited
- Catheter ablation may be a useful adjunctive therapy