Risk Stratification for SCD

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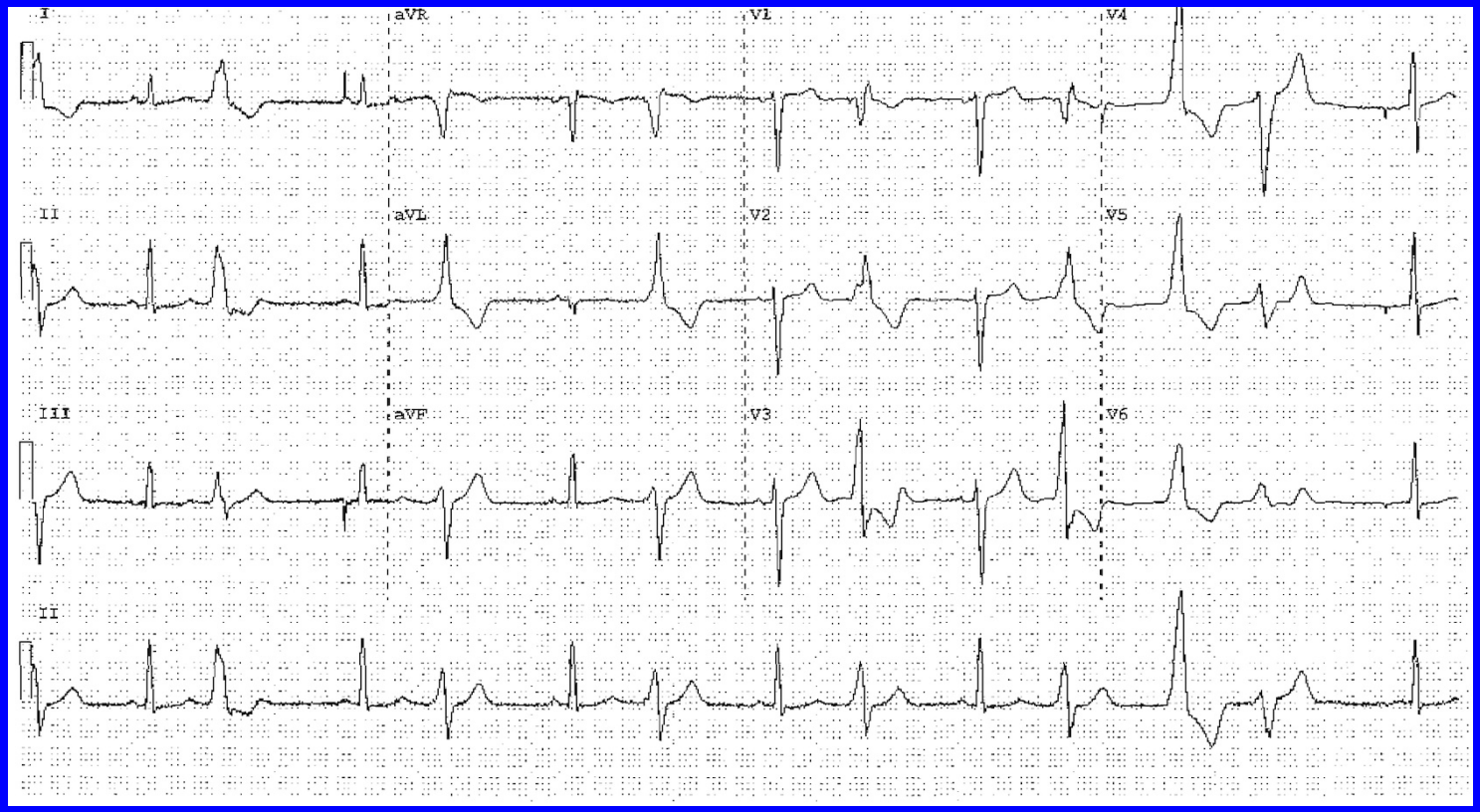
Disclosures: none

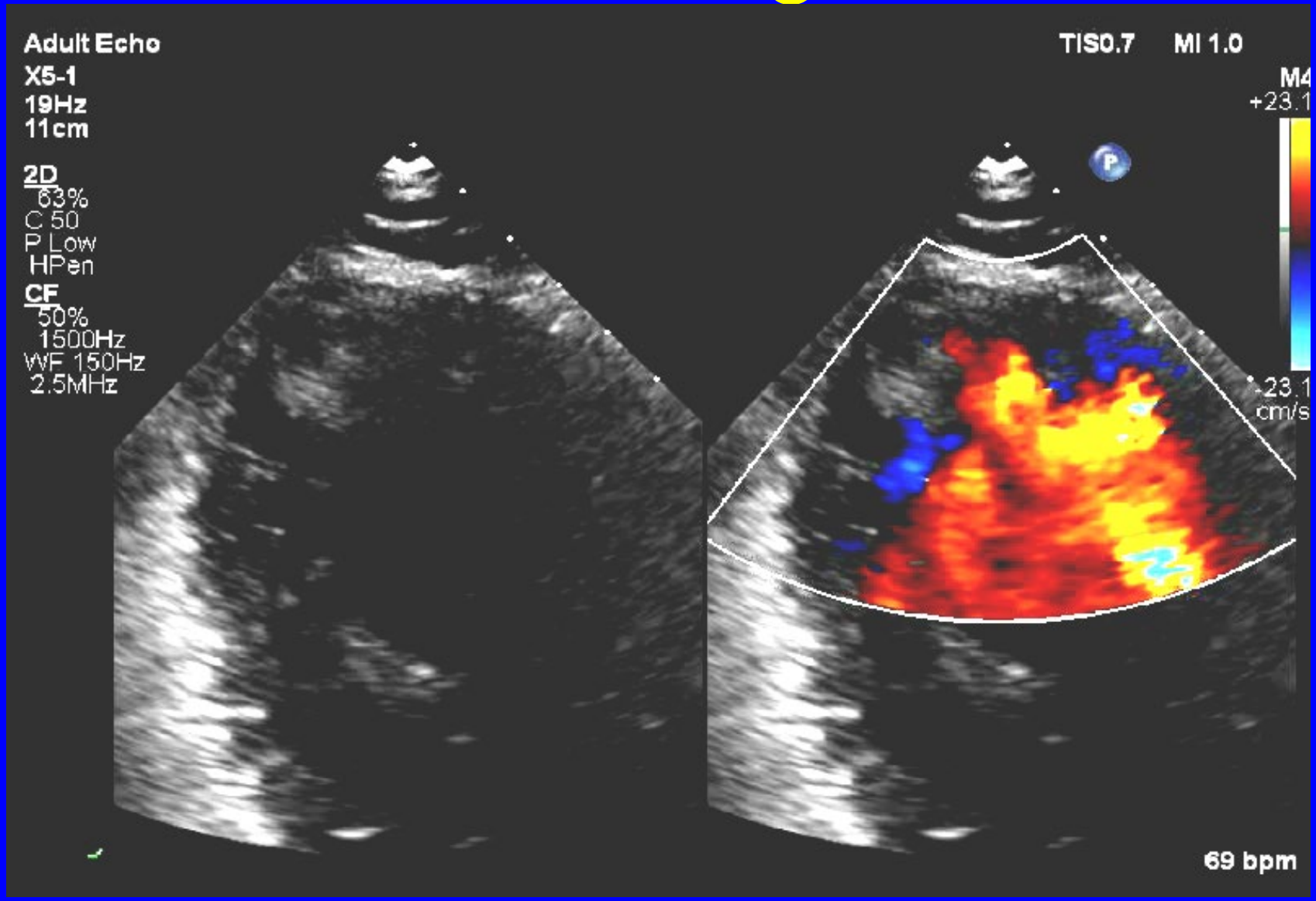
Case

- 45 y/o male with palpitations and a syncopal episode while walking on the street
- Father has Hx of NICM with VA and underwent cardiac transplantation in his 60s, siblings, children healthy
- Work-up showed:
  - Holter: frequent PVCs , PVC burden 14%, 435 runs of nsVT (up to 8 beats, rate up to 197 bpm) and 9 runs of IVRs
  - Echocardiogram: outside Echo showed LVEF of 37%
  - MRI showed decreased EF, septal DE, localized apical hypertrabeculation
- A cardiac catheterization showed nl coronary arteries
- The patient was referred for a further management

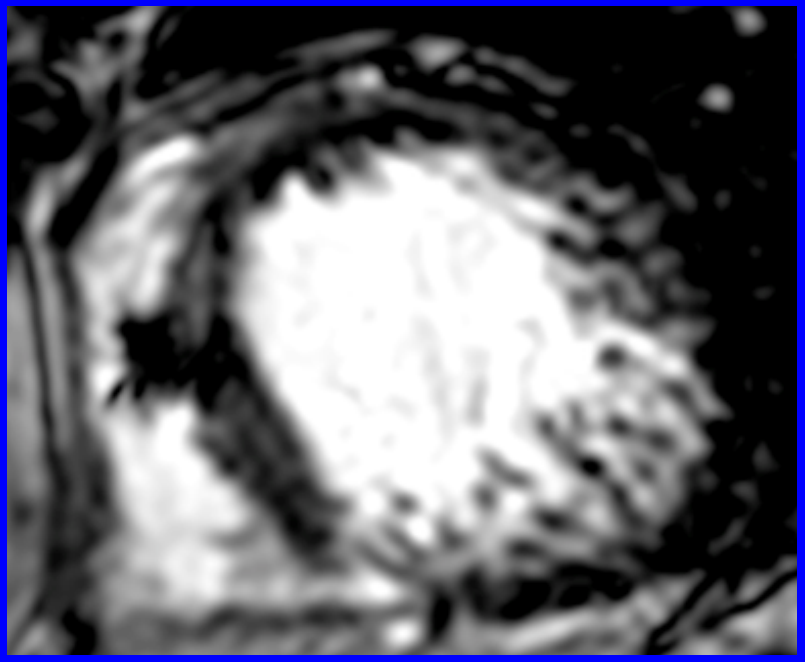
12 lead ECG



Echocardiogram

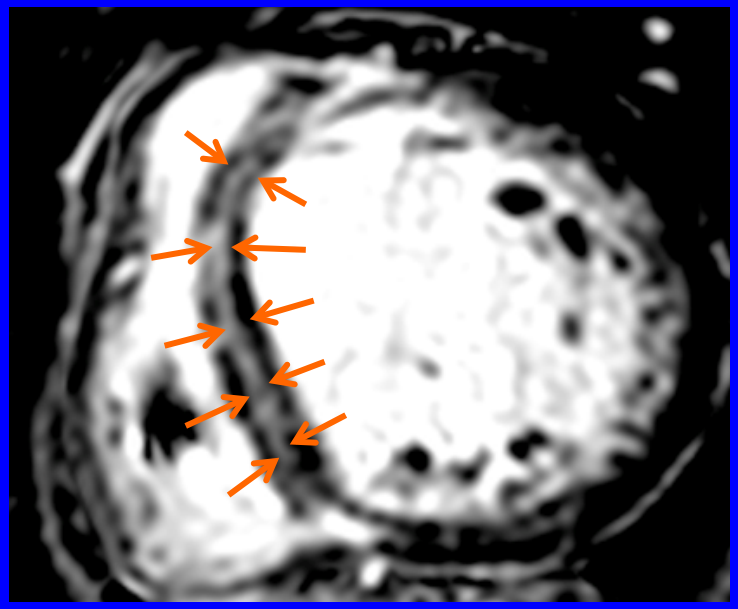


Cardiac MRI

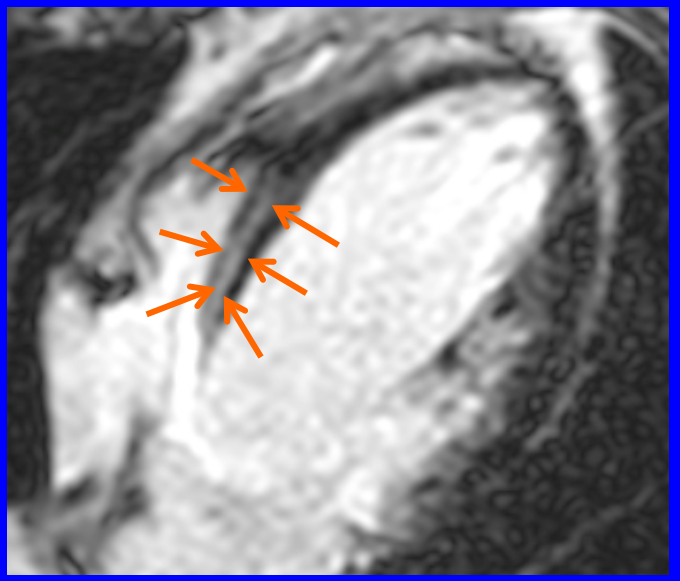


Cardiac MRI

SA



LA



What should be the next step?

A. Mapping and ablation of PVCs and reassess
B. Guideline directed therapy for heart failure
C. Programmed ventricular stimulation and ICD implantation
D. Genetic testing and therapy directed by results

Risk Stratification for SCD

- Device based therapy is typically recommended for secondary prevention of SCD
- Risk stratification for primary prevention depends on specific type of cardiomyopathy
  - ICM / DCM
  - Specific ACMs (ARVC, ALVC, Brugada, HCM, LVNC, etc.)
  - Others: MVP, Cardiac sarcoidosis, etc.

Risk Stratification

Ischemic Cardiomyopathy

Risk Stratification in ICM

Primary Prevention

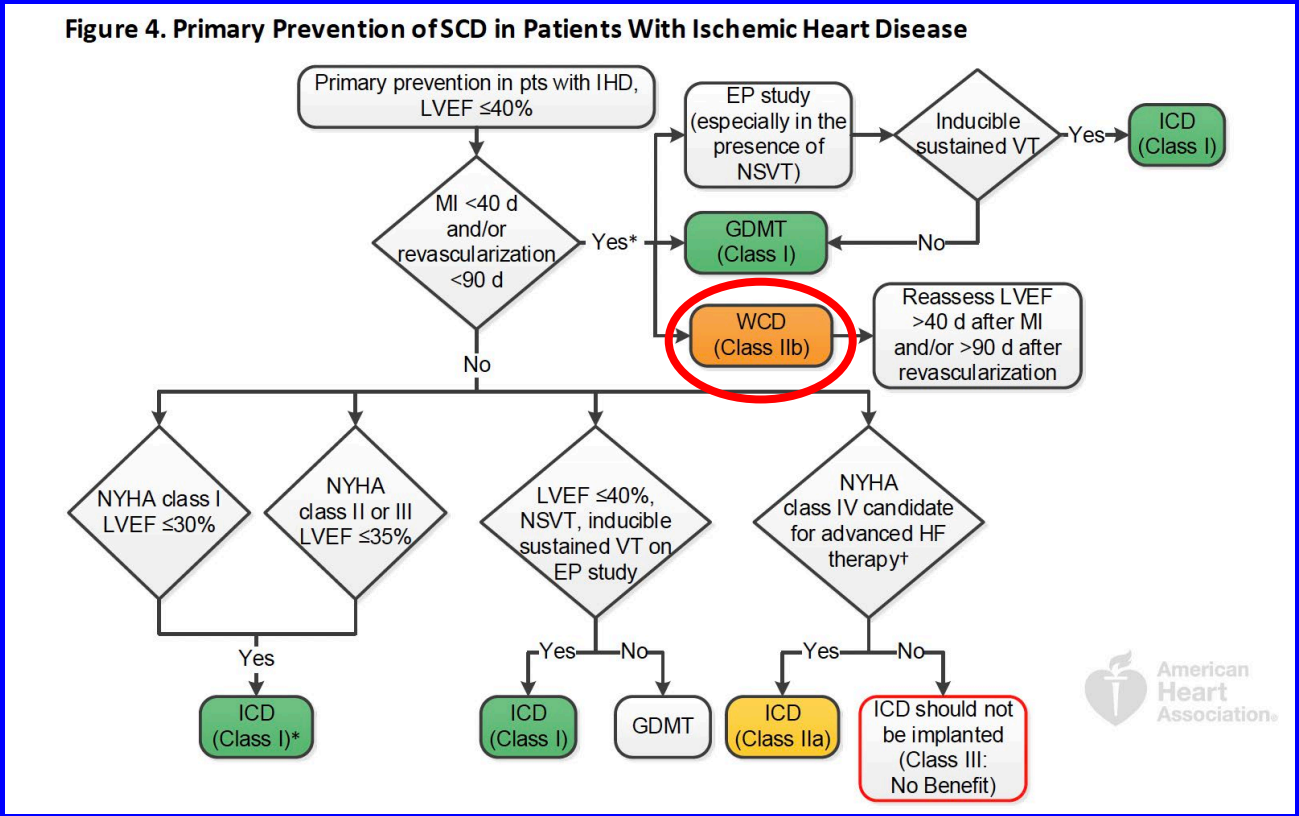
COR	LOE	Recommendations
I	A	1. In patients with LVEF of 35% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days postrevascularization, and with NYHA class II or III HF despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected (1, 2).
I	A	2. In patients with LVEF of 30% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days postrevascularization, and with NYHA class I HF despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected (2, 3).
I	B-R	4. In patients with NSVT due to prior MI, LVEF of 40% or less and inducible sustained VT or VF at electrophysiological study, an ICD is recommended if meaningful survival of greater than 1 year is expected (5).
IIa	B-NR	5. In nonhospitalized patients with NYHA class IV symptoms who are candidates for cardiac transplantation or an LVAD, an ICD is reasonable if meaningful survival of greater than 1 year is expected (6-9).
III: No Benefit	C-EO	6. An ICD is not indicated for NYHA class IV patients with medication-refractory HF who are not also candidates for cardiac transplantation, an LVAD, or a CRT defibrillator that incorporates both pacing and defibrillation capabilities.

Risk Stratification in ICM

Secondary Prevention

I	B-R B-NR	1. In patients with ischemic heart disease, who either survive SCA due to VT/VF or experience hemodynamically unstable VT (LOE: B-R) (1-4) or stable VT (LOE: B-NR) (5) not due to reversible causes, an ICD is recommended if meaningful survival greater than 1 year is expected.
I	B-NR	3. In patients with ischemic heart disease and unexplained syncope who have inducible sustained monomorphic VT on electrophysiological study, an ICD is recommended if meaningful survival greater than 1 year is expected (7).

Risk Stratification in ICM



AL-Khatib et al. ACC/AHA 2017

Risk Stratification

Idiopathic Dilated Cardiomyopathy

Risk Stratification in DCM

I	A	1. In patients with NICM, HF with NYHA class II–III symptoms and an LVEF of 35% or less, despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected (1-6).
IIb	B-R	3. In patients with NICM, HF with NYHA class I symptoms and an LVEF of 35% or less, despite GDMT, an ICD may be considered if meaningful survival of greater than 1 year is expected (5).

AL-Khatib et al. ACC/AHA 2017

Midwall LGE in Patients with DCM undergoing CMR

- Patients with suspected DCM referred for CMR and EF ≥40%
- 399 pts, median age 50, median EF 50%
- 101 patients had LGE
- 18/101patients (17.8%) had endpoint of SCD or aborted SCD compared to 7/298 patients without LGE (2.3%)
- Lack of dose response between LGE% and outcomes

Halliday, et al. Circulation 2018

Identification of the Arrhythmogenic Substrate in NICM

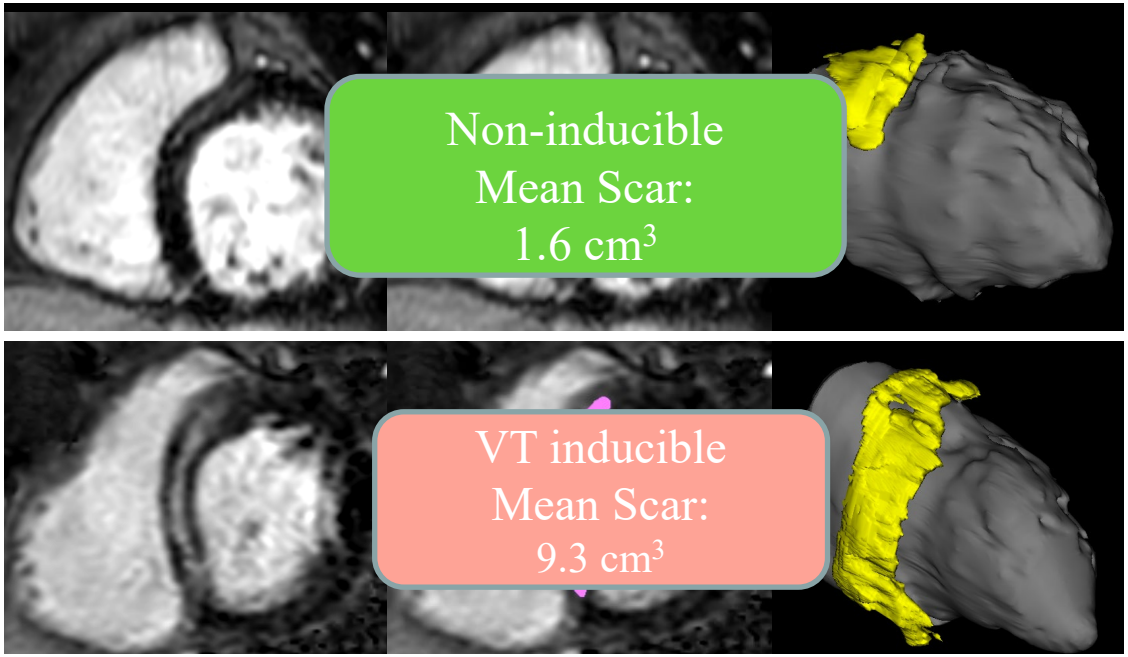
	Association with adverse outcome (VT)	Event rate	Annual ICD Therapy	Follow-up
Iles et al JACC 2009	Presence of DE	29% (9/31)	18%	1.6 yrs
Wu et al JACC 2008	Presence of DE	44% (12/27)	31%	1.4 yrs
Lehrke et al Heart 2010	- Presence of DE - DE >4% of LV mass	8% (15/72)	4%	1.9 yrs
Hombach et al Eur H J 2009	- CI - RV EDVI	25%	7%	3.6 yrs
Neilan et al JACC im. 2013	- Presence of DE - DE >4.4% of LV mass	24%	24%	2.4 yrs
Halliday et al Circulation 2018	- Presence of DE - Presence of >0% DE of LV mass	17.8%	4.45%	4.8 yrs

Risk Stratification in DCM
Imaging with CMR

IIa	B-NR	2. In patients with suspected NICM, cardiac MRI with late gadolinium enhancement can be useful for assessing risk of SCA/SCD (1-3).

AL-Khatib et al. ACC/AHA 2017

Risk stratification in NICM with frequent PVCs



Ghannam et al. : Heart Rhythm 2020

Scar volume and VT inducibility
ROC cut-off: 3.4 cm^3
AUC: 0.97, Sens. 100%, Spec. 92%

IIa	B-NR	1. CMR can be useful for risk stratification for sudden cardiac death in patients with frequent PVCs.
IIa	C-LD	2. PES can be useful for risk stratification for sudden cardiac death in patients with SHD undergoing ablation of frequent PVCs.

Cronin E, Bogun F, et al. Heart Rhythm 2019

Summary-1

- CMR defined scar is a promising imaging tool to allow risk stratification in patients with NICM
- Programmed stimulation in the presence of CMR defined scar is also promising but needs to be validated prospectively

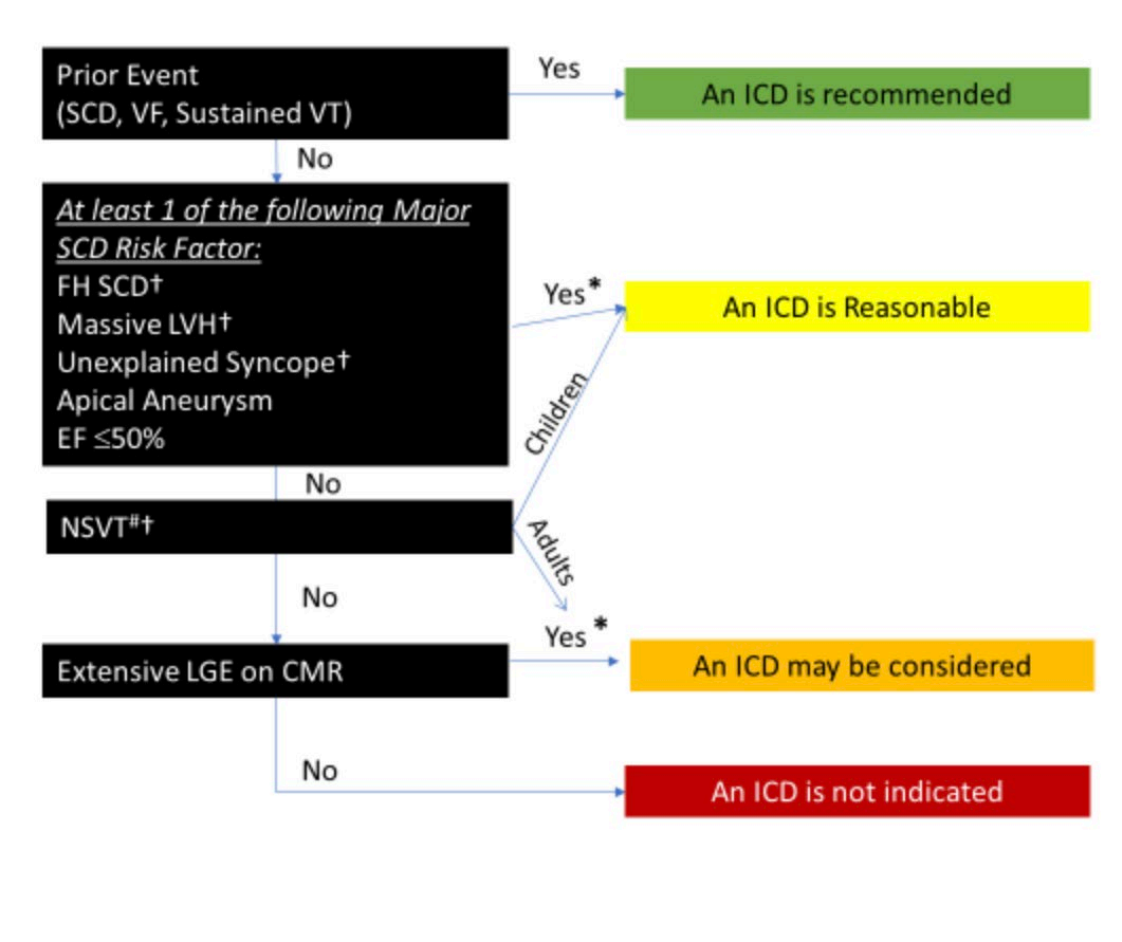
Risk Stratification

Arrhythmogenic CMP

HCM and Risk stratification

- Established Risk factors
  - Aborted SCD
  - VT causing syncope
  - Family Hx of SCD
  - LV wall thickness >30 mm
  - Unexplained syncope within 6 months
  - NSVT ≥3 beats
  - Abnormal BP response during exercise
- Risk modifiers
  - Age < 30yrs
  - DE on MRI
  - LVOT obstruction
  - Syncope > 5 yrs ago
- High Risk features
  - LV Aneurysm
  - LVEF <50%

Risk Stratification in HCM



Ommen et al. ACC/AHA 2020

ARVC and Risk stratification

ARVC and Risk stratification

IIa	B-NR	ICD implantation is reasonable for individuals with ARVC and three major, two major and two minor, or one major and 4 minor risk factors for ventricular arrhythmia.*
IIb	B-NR	ICD implantation may be reasonable for individuals with ARVC and two major, one major and two minor, or 4 minor risk factors for ventricular arrhythmia.*
IIa	B-NR	In individuals with ACM and syncope suspected to be due to a ventricular arrhythmia, an ICD is reasonable.

Major criteria: nsVT, inducible VT, EF <50%
Minor criteria: male sex, >1000 PVCs / 24hrs, RV dysfunction, probant status, 2 or more desmosomal variants

Towbin et al. Heart Rhythm 2019

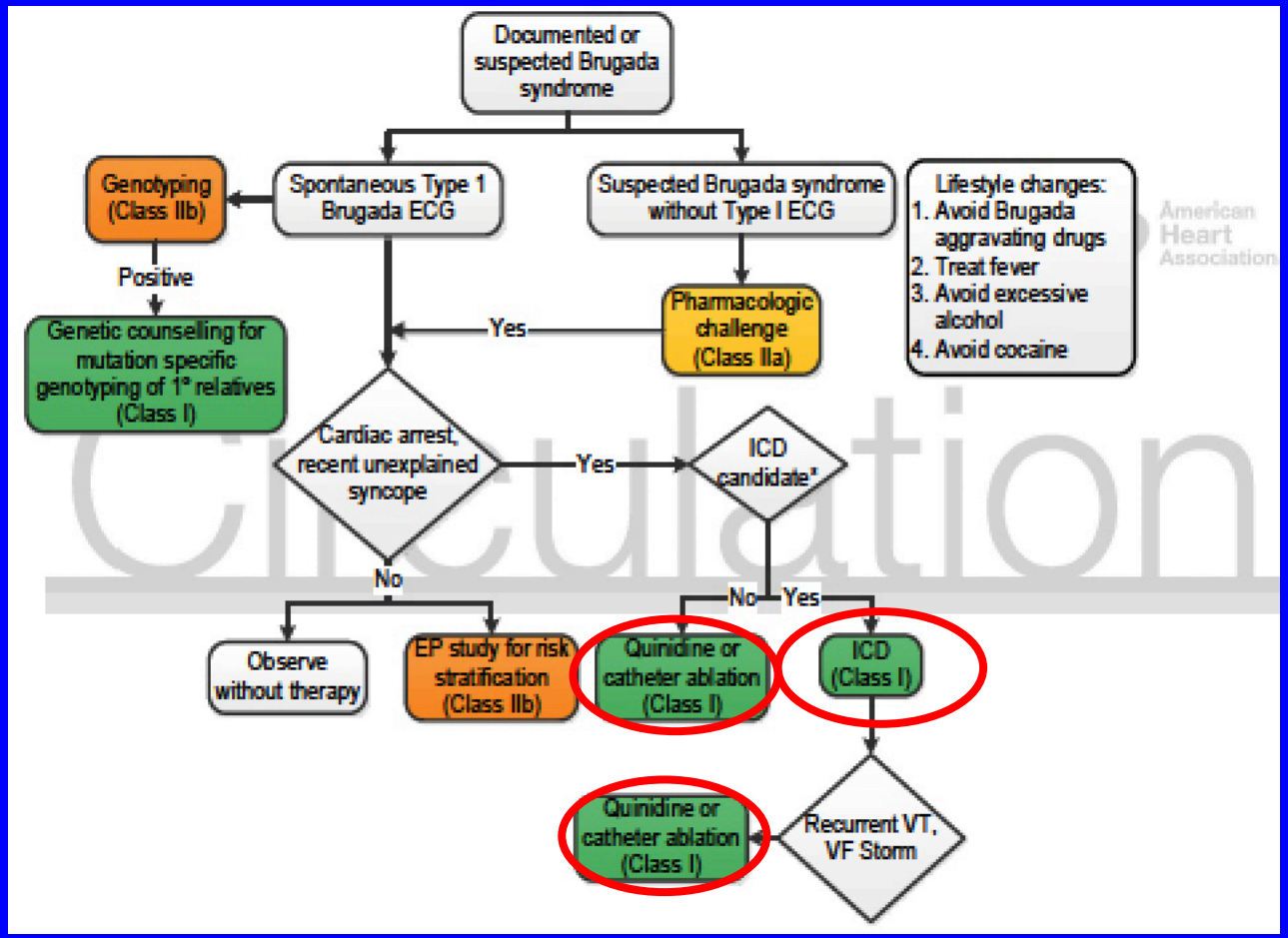
Brugada Sd and Risk Stratification

Brugada Sd and Risk stratification

Recommendations for Brugada Syndrome References that support the recommendations are summarized in Online Data Supplement 42 and Systematic Review Report.		
COR	**LOE**	**Recommendations**
I	B-NR	1. In asymptomatic patients with only inducible type 1 Brugada electrocardiographic pattern, observation without therapy is recommended.
I	B-NR	2. In patients with Brugada syndrome with spontaneous type 1 Brugada electrocardiographic pattern and cardiac arrest, sustained VA or a recent history of syncope presumed due to VA, an ICD is recommended if a meaningful survival of greater than 1 year is expected (4, 8).
I	B-NR	3. In patients with Brugada syndrome experiencing recurrent ICD shocks for polymorphic VT, intensification of therapy with quinidine or catheter ablation is recommended (7-11).
I	B-NR	4. In patients with spontaneous type 1 Brugada electrocardiographic pattern and symptomatic VA who either are not candidates for or decline an ICD, quinidine or catheter ablation is recommended (7, 9-11).
IIa	B-NR	5. In patients with suspected Brugada syndrome in the absence of a spontaneous type 1 Brugada electrocardiographic pattern, a pharmacological challenge using a sodium channel blocker can be useful for diagnosis (12-14).
IIb	B-NR[SR]	6. In patients with asymptomatic Brugada syndrome and a spontaneous type 1 Brugada electrocardiographic pattern, an electrophysiological study with programmed ventricular stimulation using single and double extrastimuli may be considered for further risk stratification (1, 6, 13, 15-17).
IIb	C-EO	7. In patients with suspected or established Brugada syndrome, genetic counseling and genetic testing may be useful to facilitate cascade screening of relatives (18-20).

AL-Khatib et al. ACC/AHA 2017

Brugada Sd and Risk stratification



AL-Khatib et al. ACC/AHA 2017

Other ACMs and Risk Stratification

Other ACMs and Risk Stratification

IIa	B-NR	In individuals with phospholamban cardiomyopathy and LVEF <45% or NSVT, an ICD is reasonable.
IIa	B-NR	In individuals with lamin A/C ACM and two or more of the following: LVEF <45%, NSVT, male sex, an ICD is reasonable.
IIa	C-LD	In individuals with FLNC ACM and an LVEF <45%, an ICD is reasonable.
IIa	B-NR	ICD implantation is reasonable for individuals with LVNC and evidence of nonsustained VT associated with a reduced ejection fraction.

Towbin et al. Heart Rhythm 2019

Summary-2

Primary prevention:

- HCM: ≥1 established criteria for ICD implantation with gaining importance of imaging
- ARVC: adjunctive criteria: inducible VT, nsVT, EF<50%
- Brugada: recent syncope due to VA in type I pattern (IIa), PVS (IIb)
- Other ACM: EF ≤35% depending on NYHA class with higher EF for phosphlamabn, lamin A/C, FLNC CMPs

MVP and Risk Stratification

Primary prevention:

- No generally accepted risk stratifiers for PP
- EPS may have a role in risk assessment
- Risk factors considered to be associated with SCD in addition to bileaflet MVP:
  - MAD
  - LGE
  - Redundant MV
  - ST/T wave abnormalities in inferior leads
  - Complex ventricular ectopy

Secondary prevention:

- SCD
- Syncope (arrhythmogenic)

Cardiac Sarcoidosis

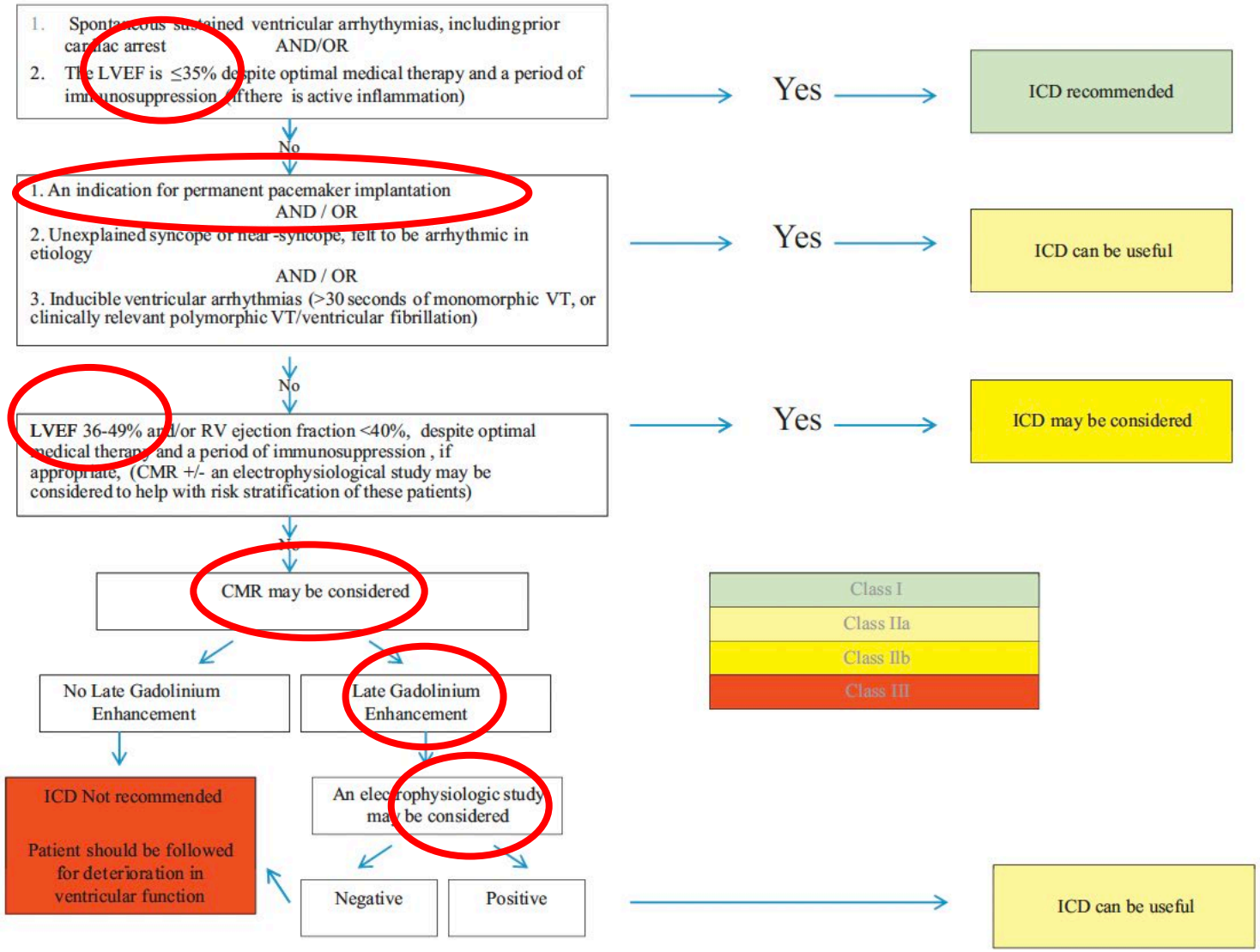
Primary prevention:

- EF<50%
- Need for pacing
- syncope
- EPS: inducible VT

Secondary prevention:

- SCD
- VT

Cardiac Sarcoidosis



Birnie et al. HRJ 2014

Case presentation

This is what was done

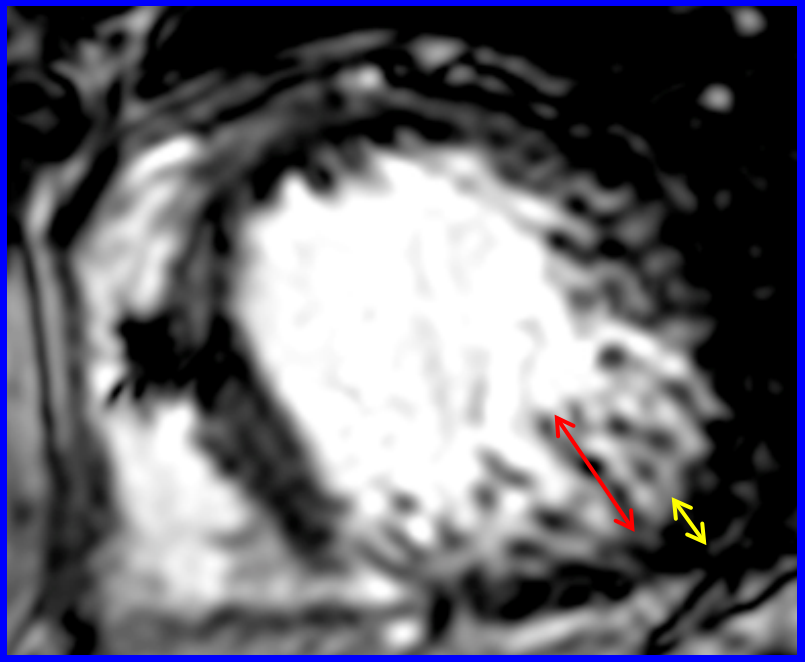
- An EP study was done and the patient had inducible sustained VT
- An ICD was implanted
- The patient tested positive for Titin mutation (TTN)
- Patient had recurrent VTs and was scheduled for ablation after AA with amiodarone failed

Diagnosis of LVNC

Diagnostic criteria for LVNC

Modality	N	LVNC Diagnostic Criteria
Echo	8	2 layers, excessively prominent ventricular trabeculations, progressively increased total myocardial wall thickness from mitral valve and toward the apex, CM/(NCM + CM) $\leq$0.5 at end-diastole (short-axis parasternal and/or apical views)
Echo	34	2 layers, intertrabecular recesses by CFD, no co-existing structural abnormality, NC/C layer $\geq$2
Echo	62	>3 trabeculations protruding from LV wall apically to papillary muscle. End-diastolic NC/C layer $\geq$2
MRI	7	2 layers, End-diastolic NC/C >2.3
MRI	16	Total LV trabeculated mass without papillary muscles. End-diastolic NC layer volume >20%

Cardiac MRI



Genetic testing

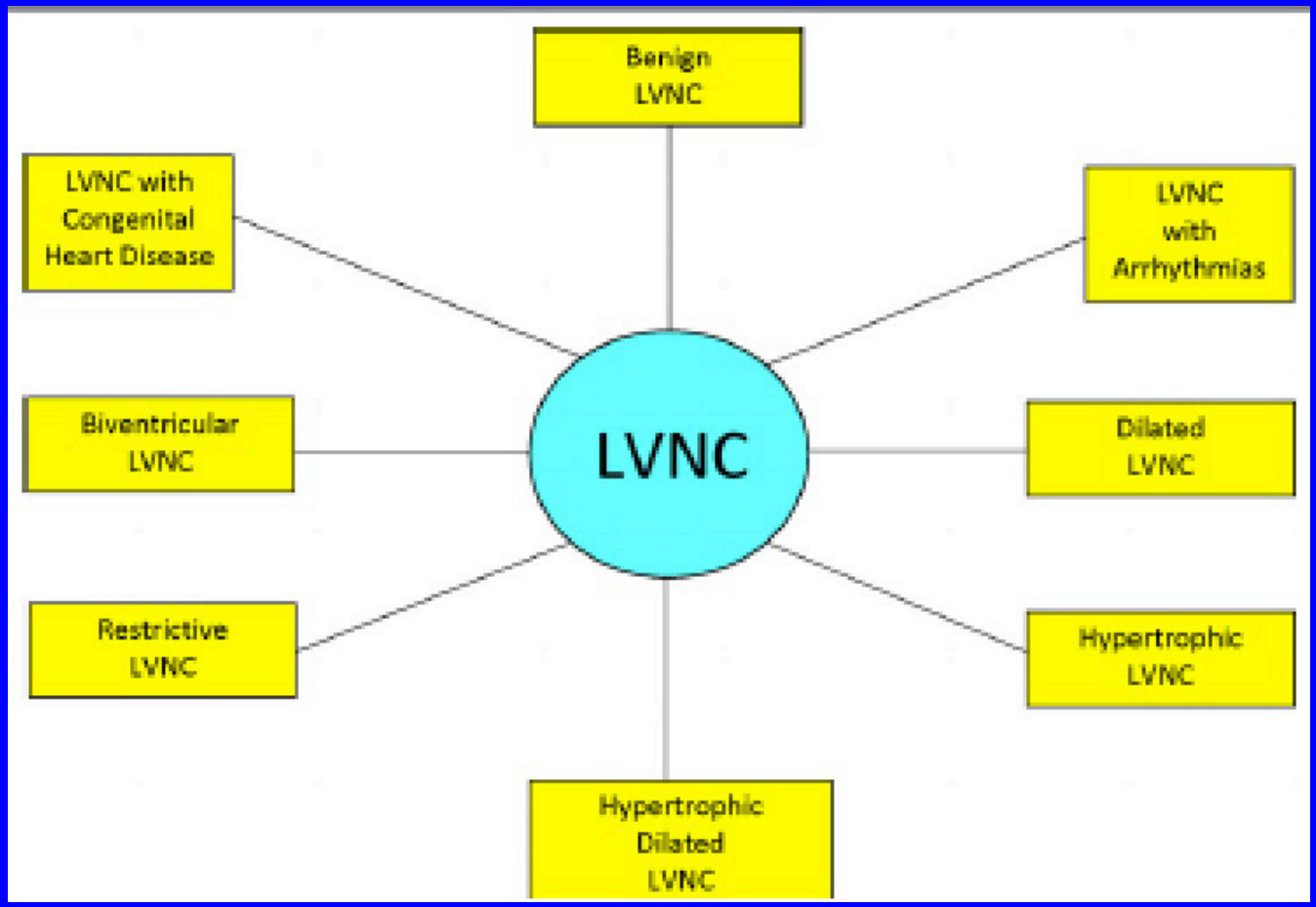
- LVNCT is genetically heterogeneous disease (AD,AR, X-linked)
- 30-50% of patients with LVNC have pathologic genetic testing
- Mutations in myosin HC MYH7, myosin binging protein gene MYBPC3 and titin gene account for most mutations (~70%)
- Patients with multiple mutations , especially titin mutation have worse outcomes: CHF, SCD.

Risk Stratification

- 23 patients with LVNC with VA (EF 39±14%) referred for ablation of VAs
- 8/23 patients had DE on CMR
- 7/8 patients with DE on CMR had inducible VT
- In 17 patients frequent PVCs were targeted:
  - 12/17 ablations were effective (71%)
  - PVC burden reduced from 25±16% to 2±3.5% ($p<0.001$)
  - EF improved to 57±8% in patients with effective ablations

Gunda, JCE 2021

Forms of LVNC



Summary-case

- CMR and echo are key for the diagnosis of LV NC
- LVNC can cause malignant VA resulting in SCD
- Genetic testing and CMR and LVEF beneficial in identifying a malignant phenotype
- Programmed stimulation beneficial in identifying malignant phenotype
- PVCs may deteriorate LV dysfunction in patients with benign and malignant LVNC