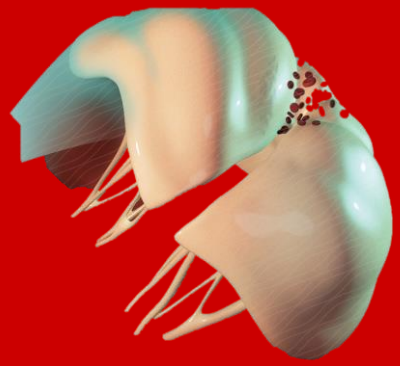


Arrhythmic mitral valve prolapse: risk stratification

Patrick Badertscher, 20.10.22, 5. Kardiologie Forum

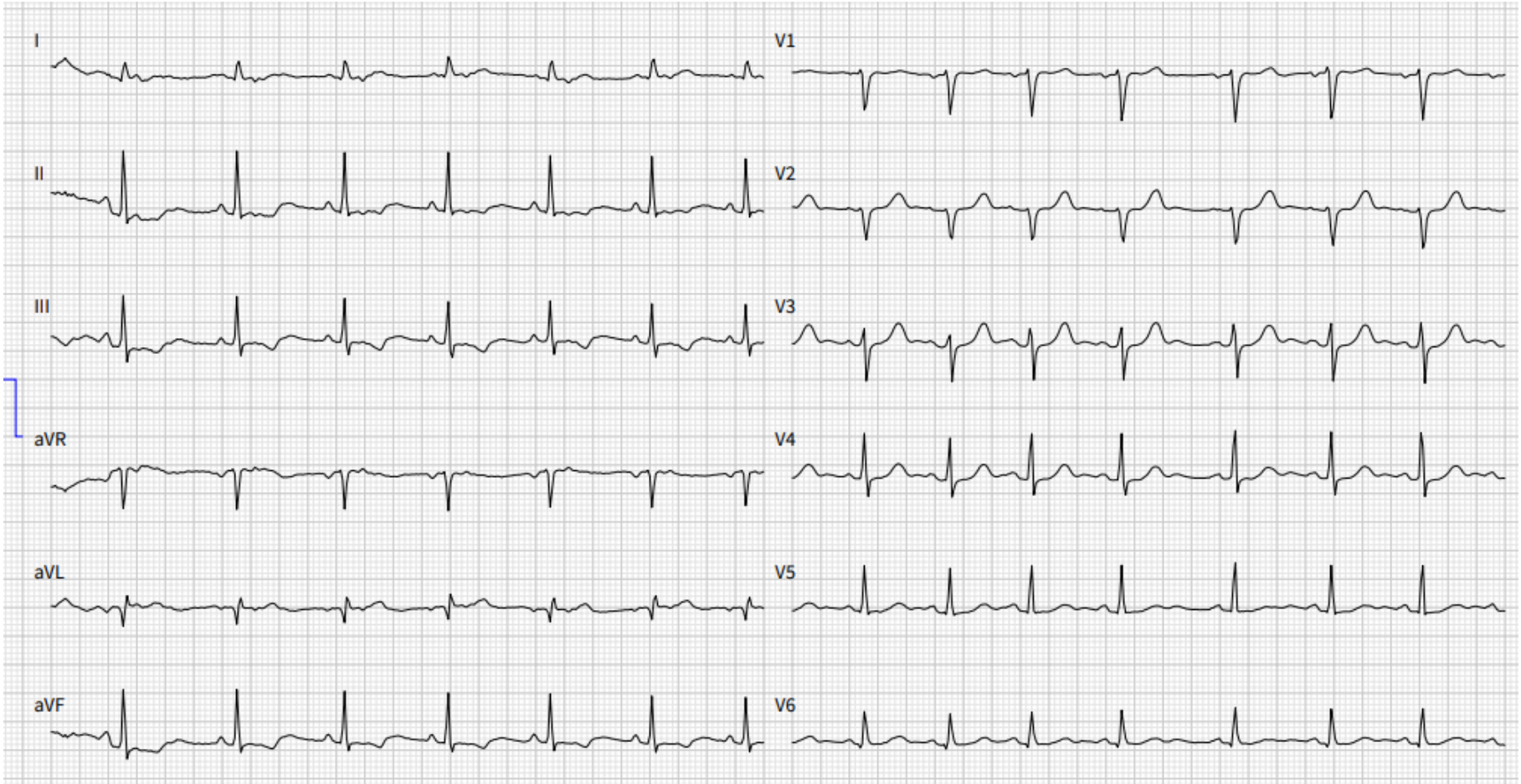
CRIB Cardiovascular Research Institute Basel

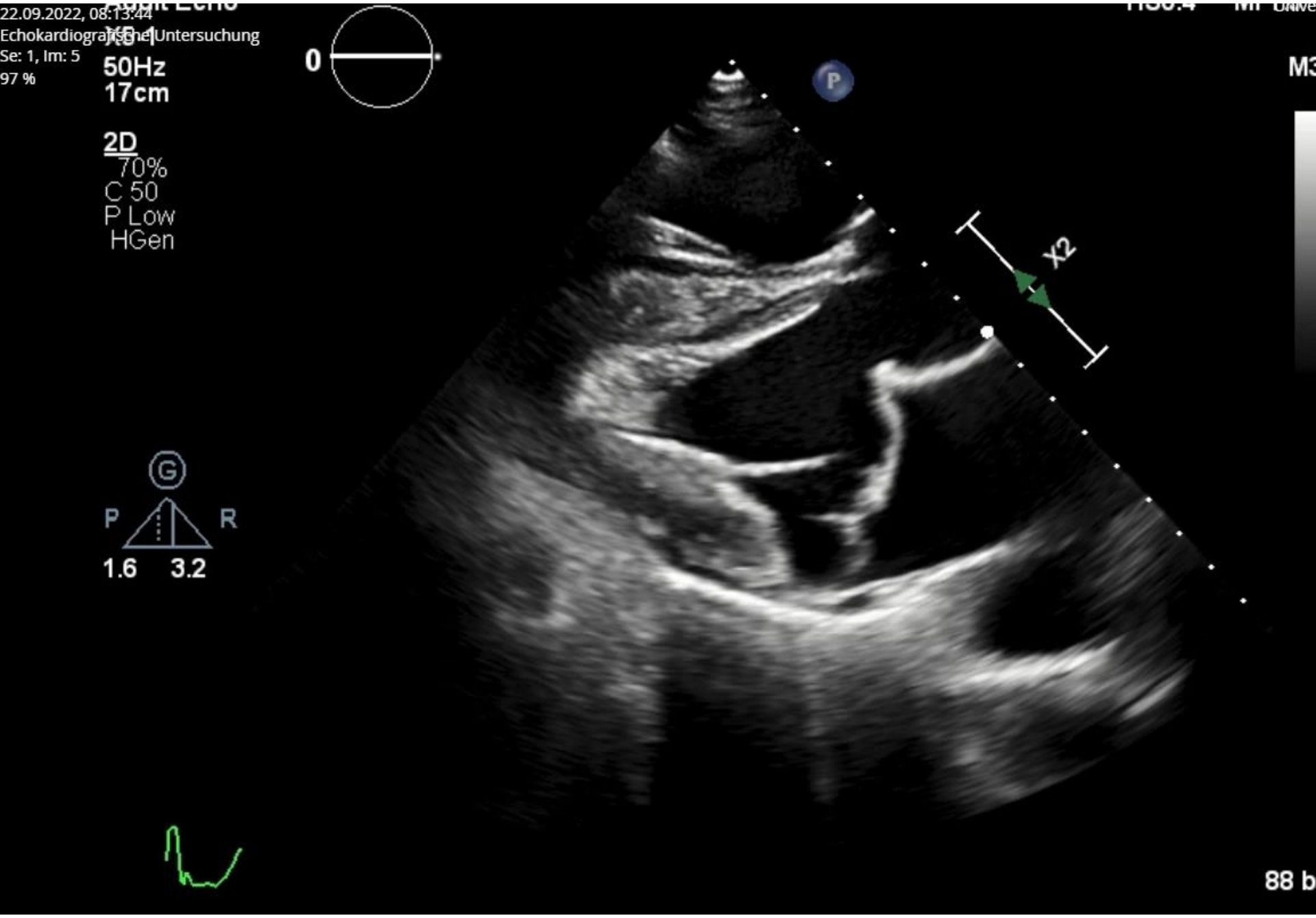
Basel Wearable Study

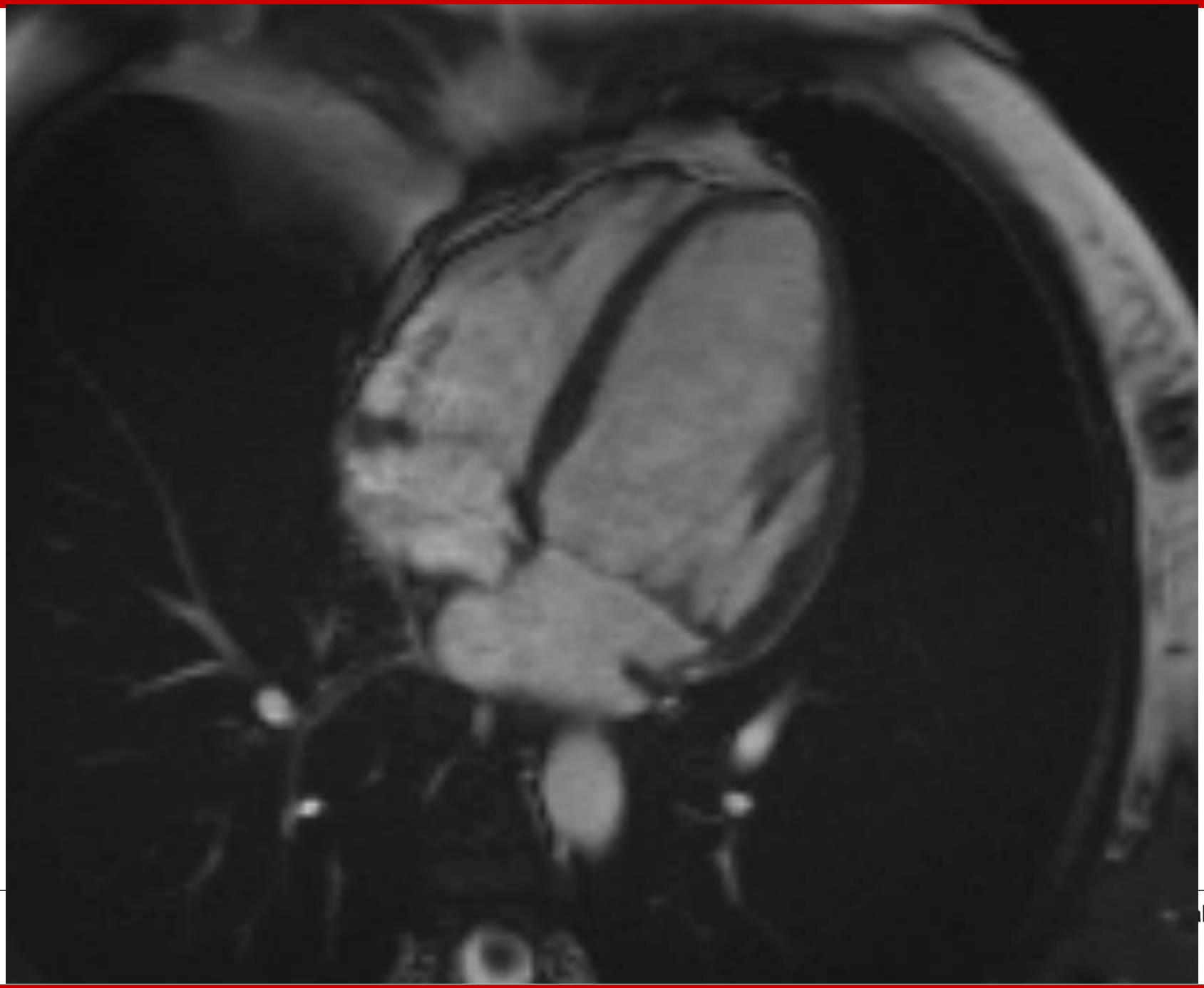
AiCM Registry

University Hospital Basel

Case: 25 yo female with palpitations




22.09.2022, 08:13:44
Echokardiographische Untersuchung
Se: 1, Im: 5
97 %
50Hz
17cm
2D
70%
C 50
P Low
HGen
0
P
X2
G
P
R
1.6
3.2
88 b



Causes of SCD in 387 Athleses

Cause	No. of Athletes	Percent
Hypertrophic cardiomyopathy	102	26.4
Commotio cordis	77	19.9
Coronary artery anomalies	53	13.7
Left ventricular hypertrophy of indeterminate causation†	29	7.5
Myocarditis	20	5.2
Ruptured aortic aneurysm (Marfan syndrome)	12	3.1
Arrhythmogenic right ventricular cardiomyopathy	11	2.8
Tunneled (bridged) coronary artery‡	11	2.8
Aortic valve stenosis	10	2.6
Atherosclerotic coronary artery disease	10	2.6
Dilated cardiomyopathy	9	2.3
Myxomatous mitral valve degeneration	9	2.3
Asthma (or other pulmonary condition)	8	2.1
Heat stroke	6	1.6
Drug abuse	4	1.0
Other cardiovascular cause	4	1.0
Long QT syndrome§	3	0.8
Cardiac sarcoidosis	3	0.8
Trauma causing structural cardiac injury	3	0.8
Ruptured cerebral artery	3	0.8

*Data are from the registry of the Minneapolis Heart Institute Foundation (3). †Findings at autopsy were suggestive of HCM but were insufficient to be diagnostic. ‡Tunneled coronary artery was deemed the cause of death in the absence of any other cardiac abnormality. §The long QT syndrome was documented on clinical evaluation. Source: Reproduced from Maron B.J. (3) with permission of the Massachusetts Medical Society.

Maron BJ, NEJM 2003

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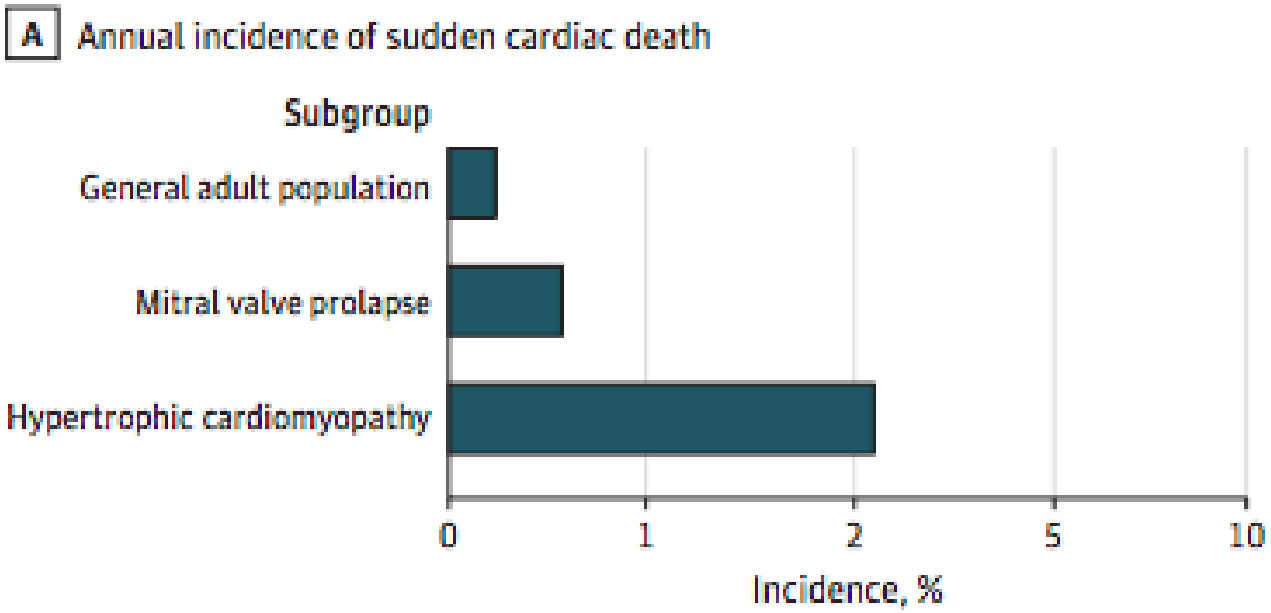
Arrhythmic MVP: Incidence and at risk



MVP-Related SCD:

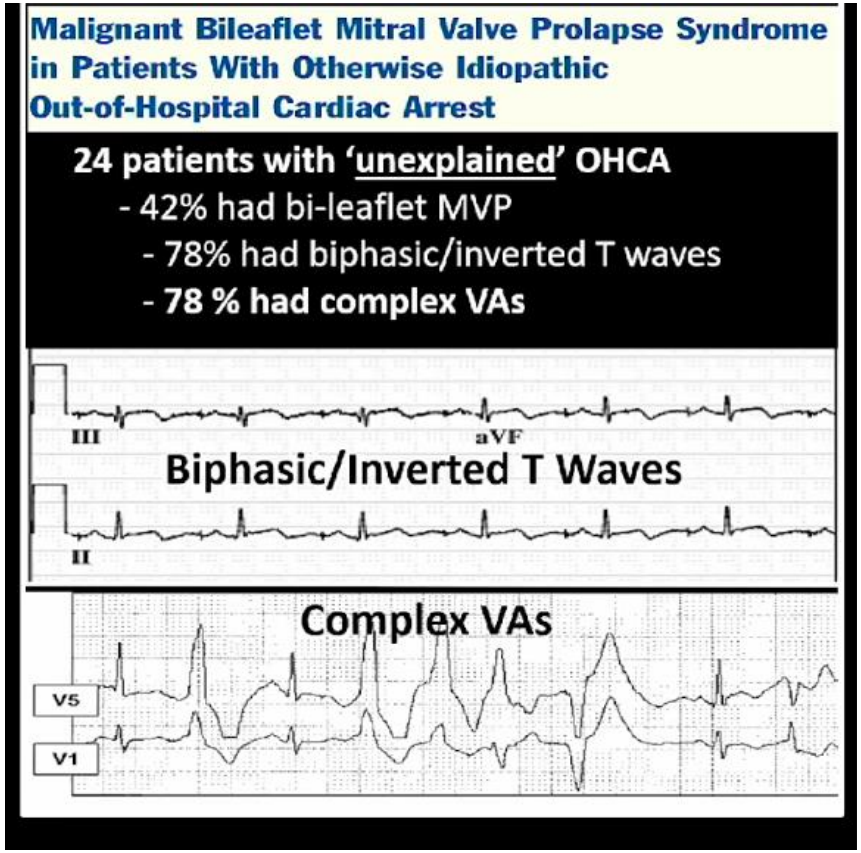
- 3x risk of general population
- Estimated risk is 0.2% to 1.8%

Muthukumar et al, JAMA Cardiology 2020

Multimodality approach for evaluation of SCD in MVP

Modality	Parameter	Condition Associated with Increased Risk
ECG/Holter		
Echo		
CMR		
PET-MRI		

Majority of MVP-SCD exhibited complex ventricular ectopy



Sriram CS et al, JACC 2013 and Basso C et al, Circulation 2015

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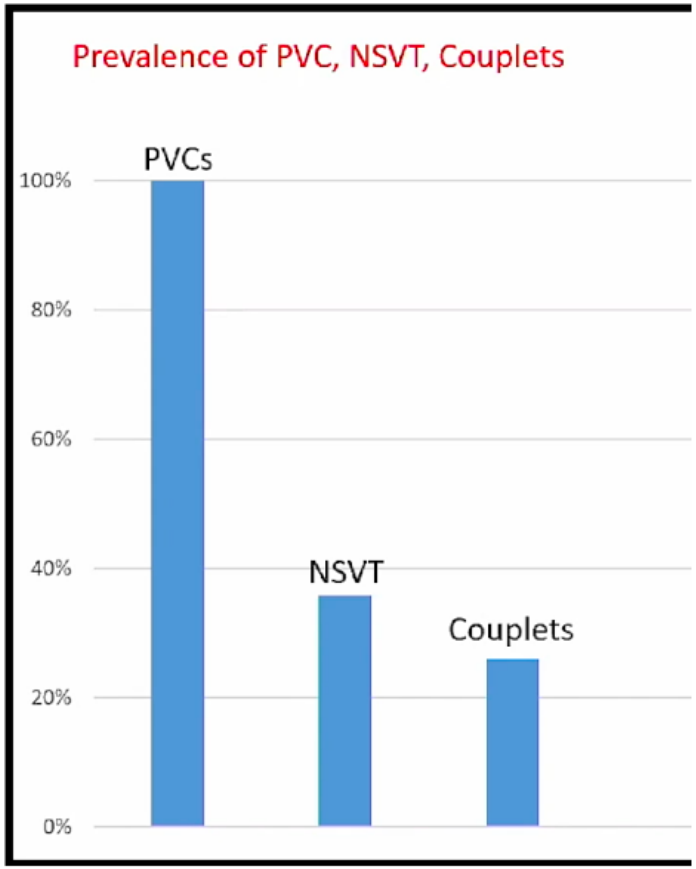
Survivors of MVP-related SCD



Hourdain J et al, Circulation 2018

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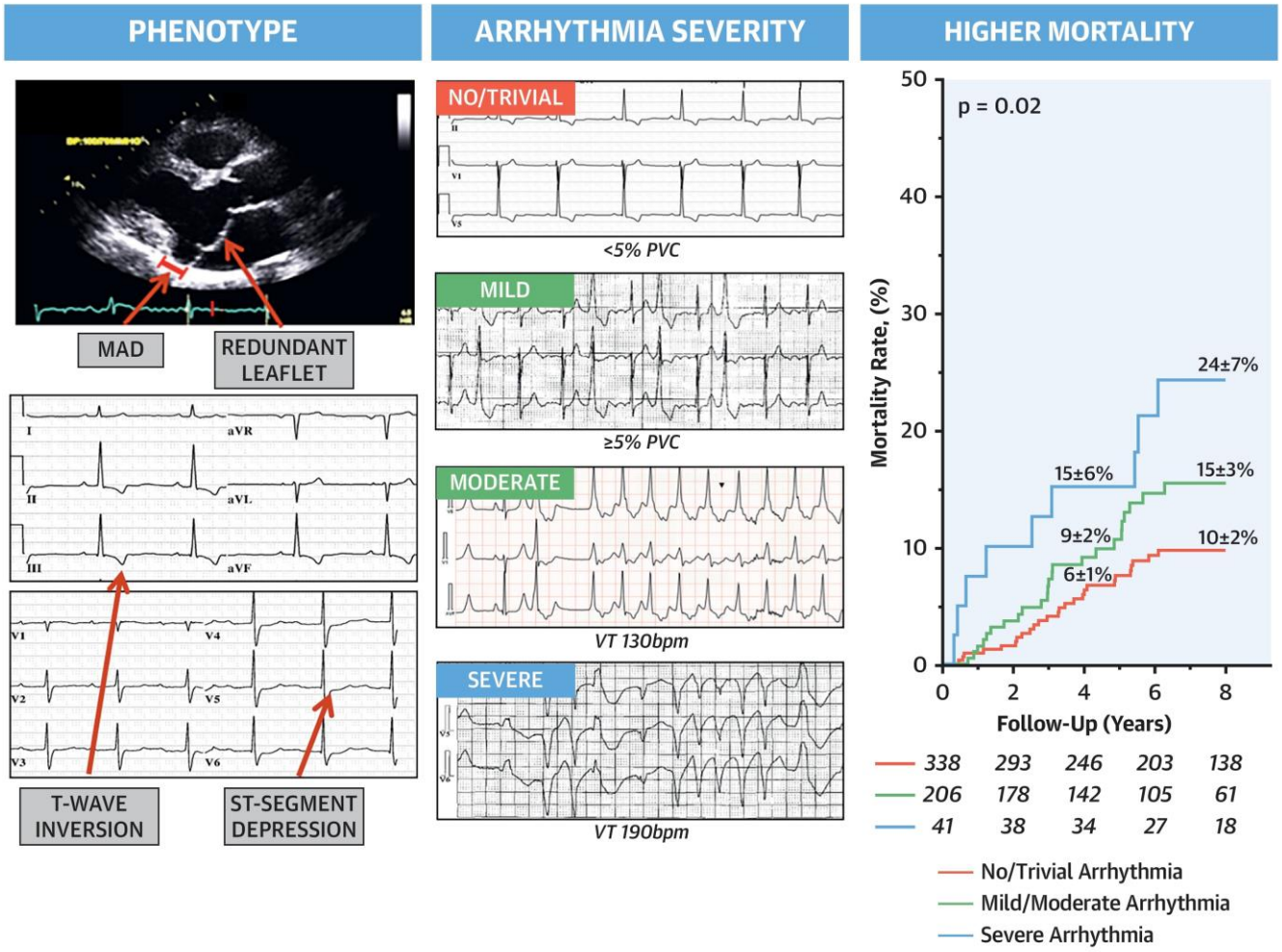
PPM
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

Mortality in Arrhythmic MVP: Stratified by VA Severity



Essayagh B et al, JACC 2020

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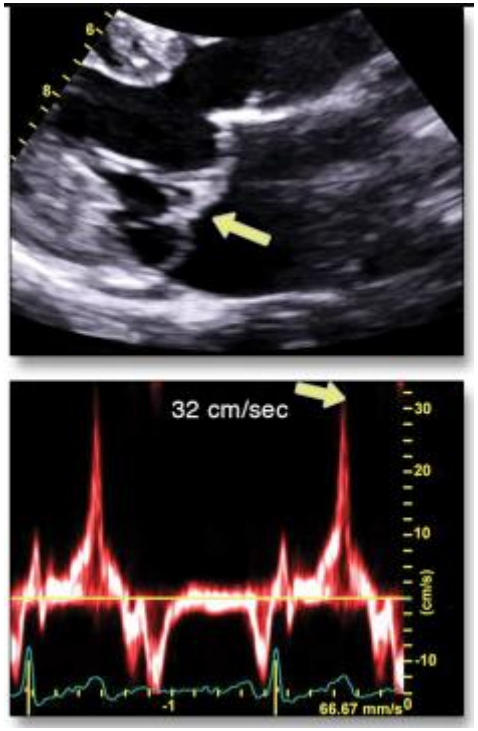
PVC and MVPs

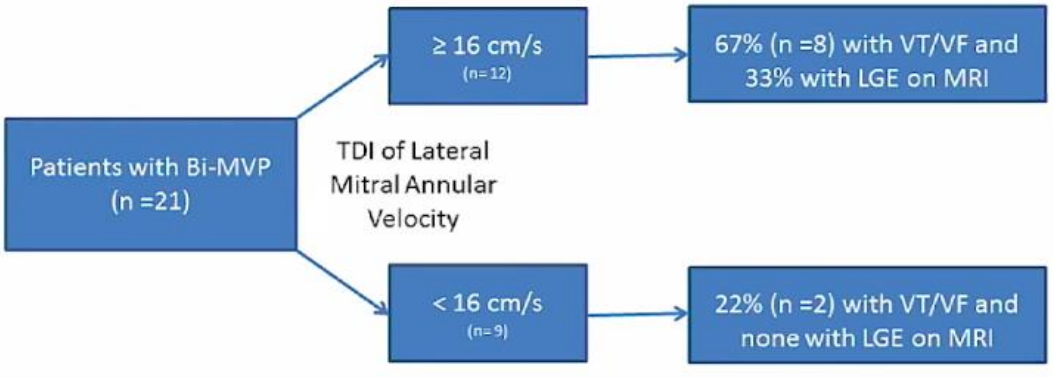
- PVCs are a trigger and likely also reflect an arrhythmogenic substrate
- PVCs are common in all MVP patients, but almost universally observed in patients who expereiced VT/VF
- Complex PVCs, including a papillary muscle morphology, warrants further evaluation

Multimodality approach for evaluation of SCD in MVP

Modality	Parameter	Condition Associated with Increased Risk
ECG/Holter	PVCs	-> Presence of PVCs -> Pap Muscle Origin -> Complex VAs: couplets, triplets, pleo
Echo		
CMR		
PET-MRI		

Pickelhaube Sign: Spiked Lateral S‘





Muthukumar et al, JACC Imaging 2016

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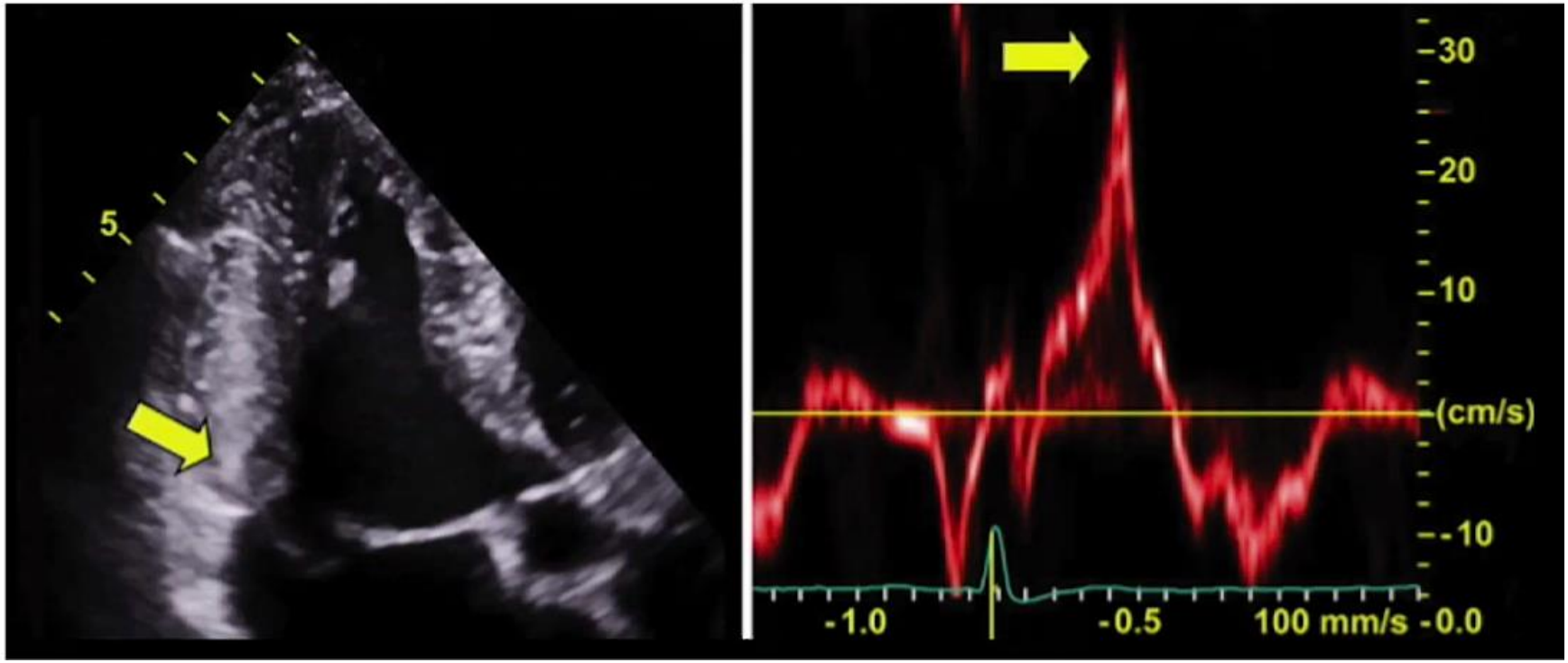
Pickelhaube Sign: Spiked Lateral S‘



- Highest Pickelhaube signal velocity in the posterolateral anulus (AP3C)
- A cut-off of 19 cm/s has a specificity of 72%
- Presence of Pickelhaube sign doubles risk of developing VT (OR 2.02)

Ignatoswiski et al, JASE 2020

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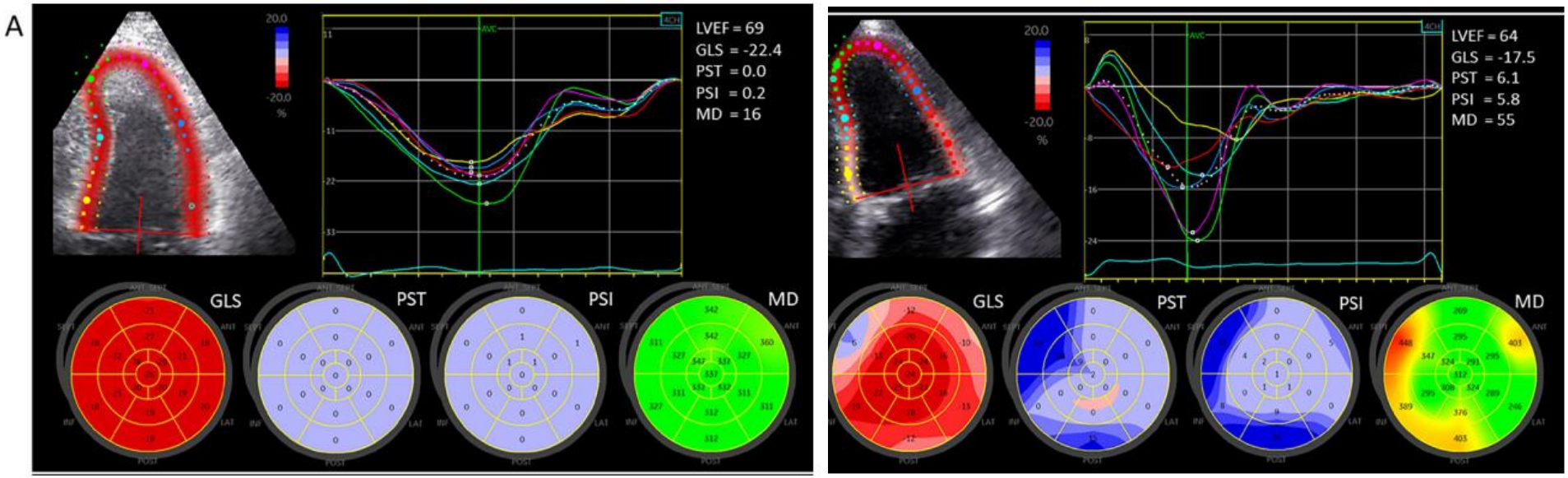
Strain Imaging: One more piece to the puzzle



Wijngaarden et al, Heart 2021

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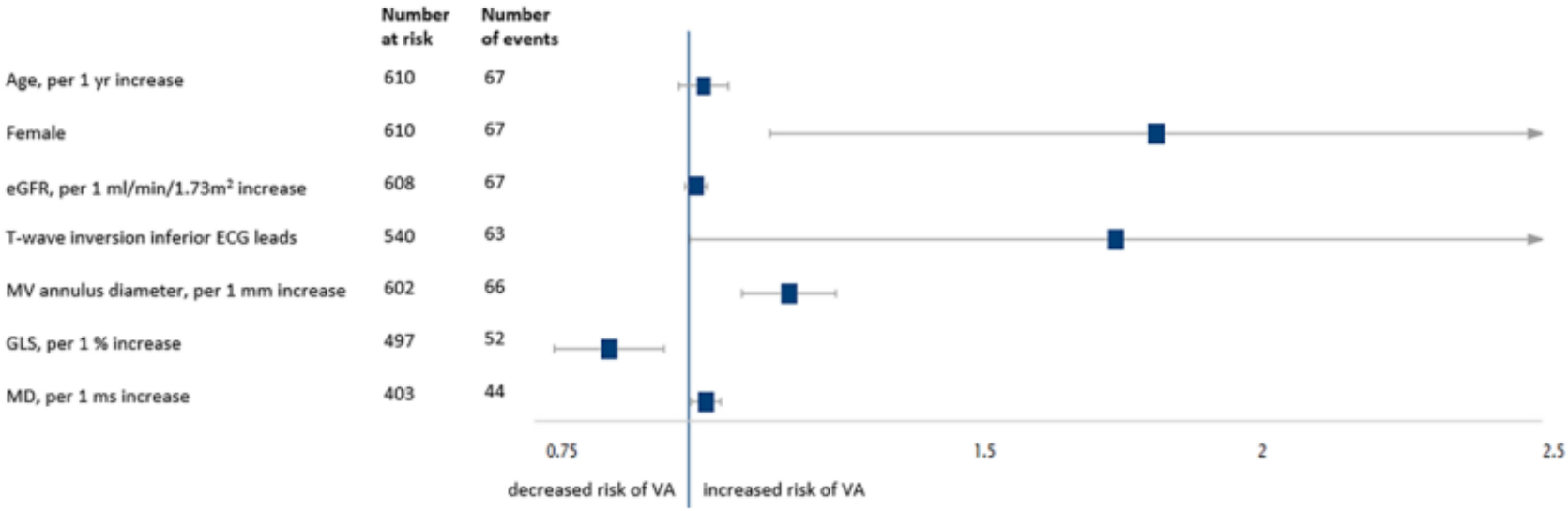
Strain Imaging in MVP: One more pice to the puzzle

- Subtle LV function impairment (GLS) is associated with symptomatc VAs
- 610 patients with MVP and ≥ moderate MR
- Symptomatic VA: frequent PVCs, NSVT or sustained VT/VF



Wijngaarden et al, Heart 2021

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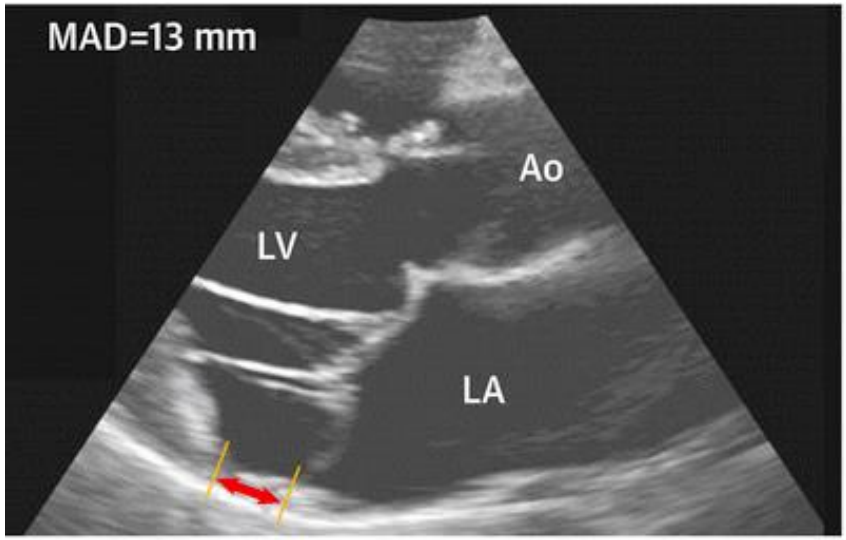
Strain Imaging in MVP: One more pice to the puzzle

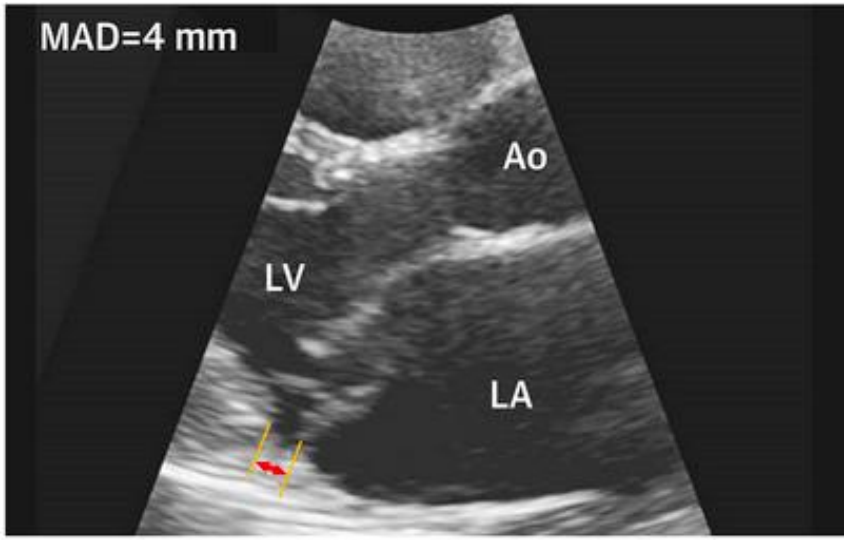
- Abnormal GLS associated with VA in multiple other arrythmic substrates
- Abnormal GLS seems to be associated with more VAs in patients with MVP
- Precise cut-off which can discriminate high from low is unknown
- Strain imaging allows to measure mechanical stress and fibrosis (even before development?)

Huttin et al, EHJ Cardiovascular Imaging 2017

Mitral Anular Disjunction

Detachment of the roots of the anulus from the ventricular myocardium





- Prevalence of MAD = 16% in patients with MVP and significant MR
- Correlation between degree of MAD (lenght) and amount of LGE (fibrosis)
- Severity of MAD is correlated with the occurence of NSVT

Mantegazza et al, JACC Imaging 2019

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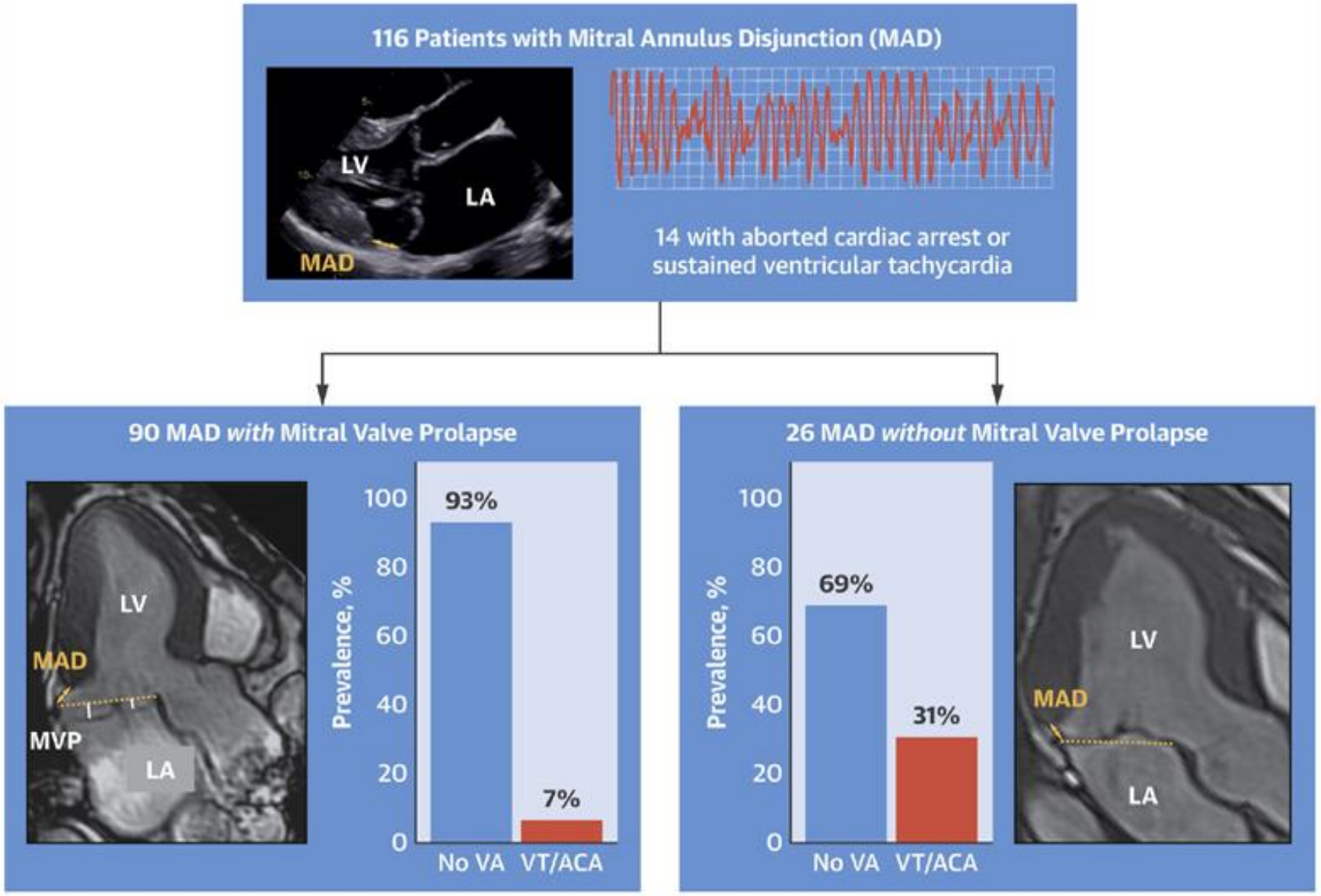
CENTRAL ILLUSTRATION: Mitral Annulus Disjunction (MAD) Arrhythmic Syndrome



Dejgaard, L.A. et al. J Am Coll Cardiol. 2018;72(14):1600-9.

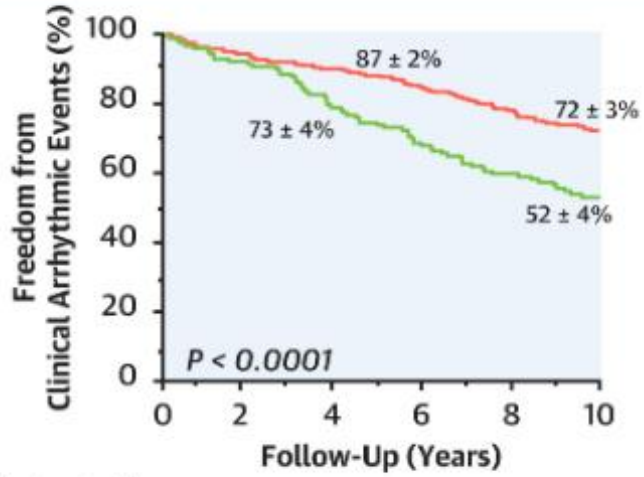
CENTRAL ILLUSTRATION: Mitral Annular Disjunction Phenotype and Outcome in Degenerative Mitral Regurgitation

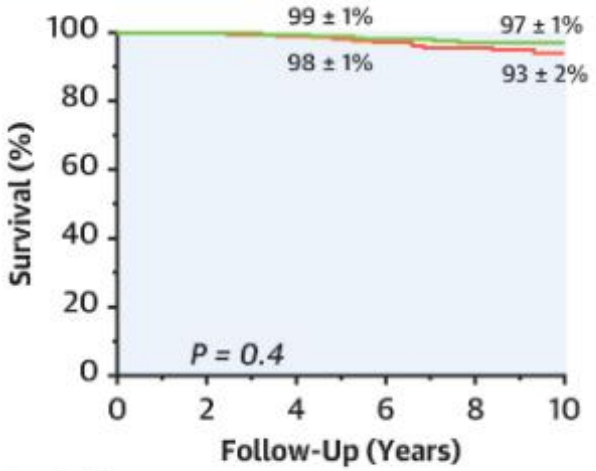
MAD PHENOTYPE

Younger age
Larger LV
Redundant leaflets
Bileaflet MVP

MITRAL ANNULAR DISJUNCTION

LONG-TERM OUTCOME





Patients at risk						
No MAD	300	280	268	249	211	151
MAD	135	123	107	92	77	57

Patients at risk						
No MAD	185	185	184	180	145	87
MAD	179	179	179	176	147	90

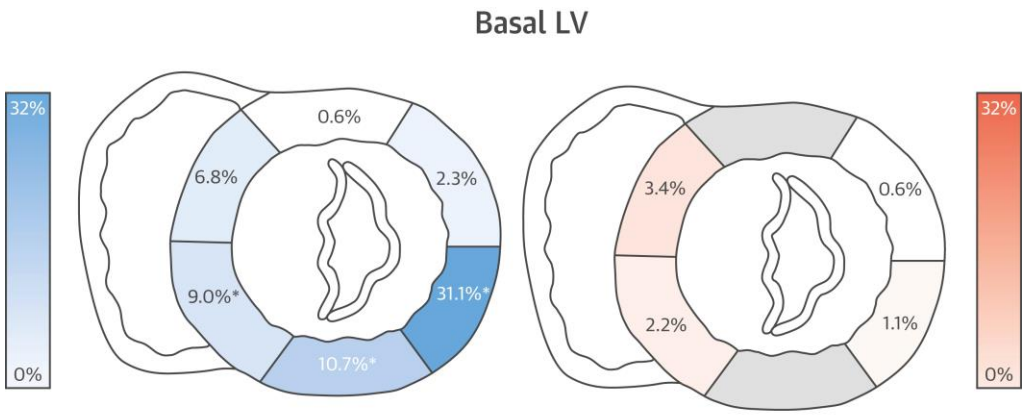
Essayagh, B. et al. J Am Coll Cardiol Img. 2021;14(11):2073-87.

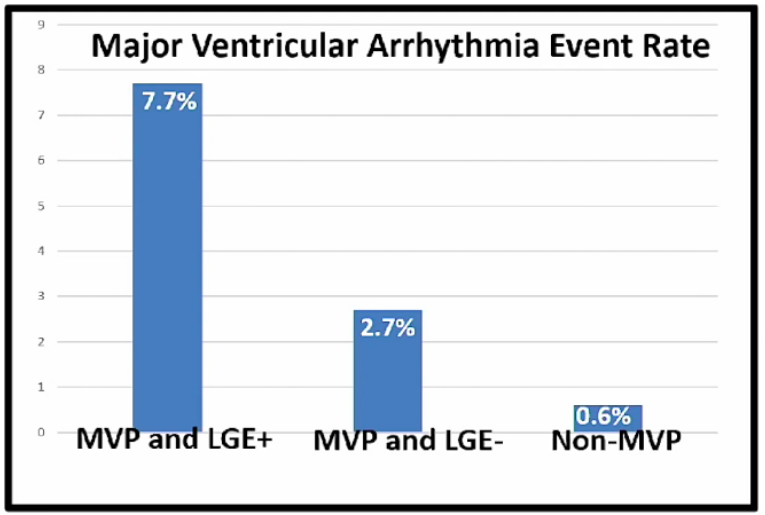
Multimodality approach for evaluation of SCD in MVP

Modality	Parameter	Condition Associated with Increased Risk
ECG/Holter	PVCs	-> Presence of PVCs -> Pap Muscle Origin -> Complex VAs: couplets, triplets, pleo
Echo	Tissue Doppler MAD Strain Mechanical Dispersion	-> Pickelhaube -> longer MAD length -> Impaired global longitudinal strain -> Greater mechanical dispersion
CMR		
PET-MRI		

Myocardial fibrosis

- Most commonly focal (replacement fibrosis)
- Typically localized to the basal inferolateral wall / pap muscle
- Presence associated with major VAs





Nearly one-third of MVP patients had replacement fibrosis in the basal Inferolateral segment (adjacent to the PMP)

Kitkungyan D et al, JACC 2018

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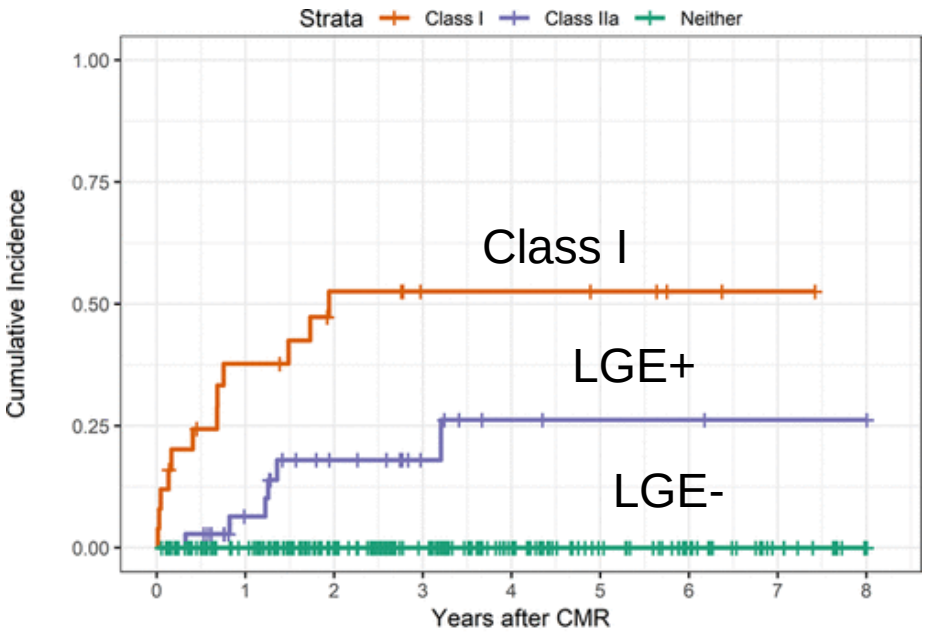
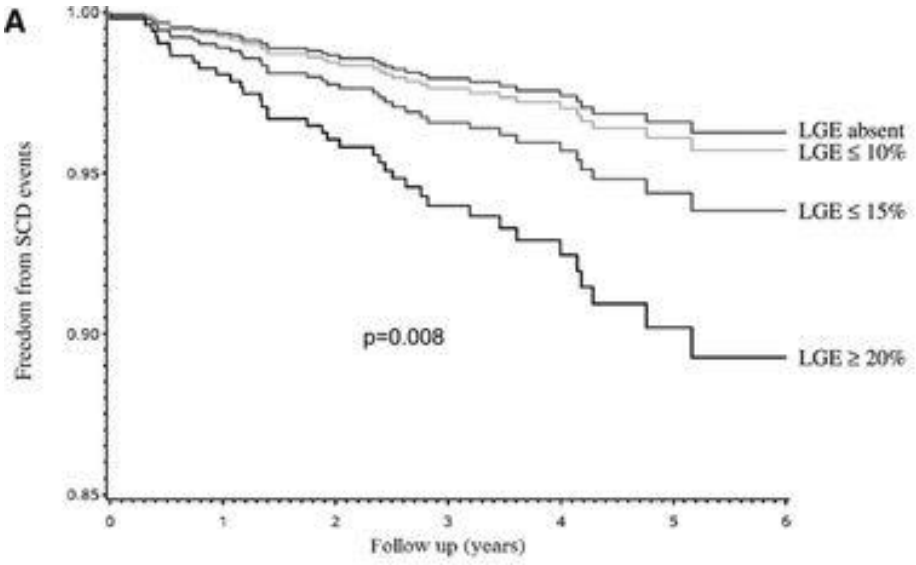
Scar (LGE) and MVP

Future studies will determine whether burden of scar enhances risk stratification in patients with MVP as it does for other substrates assoicated with SCD



Sarcoidosis



HCM

Kazmirczak et al, Circ A&E 2019 *Chan RH et al, Circ 2014*

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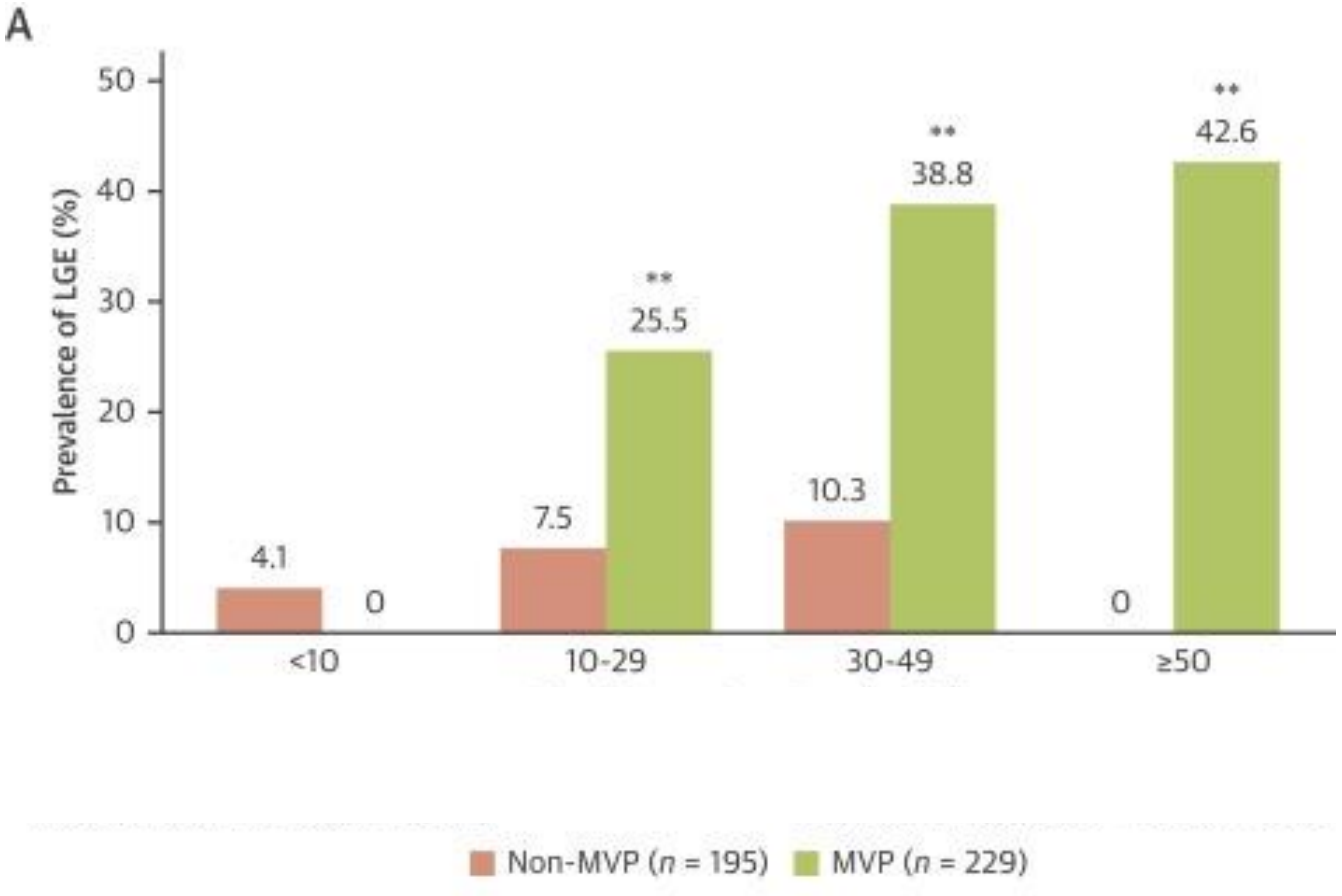
Replacement fibrosis is common in MVP



Replacement fibrosis is present in 25% of patients with mild MR

Kitkungvan et al, JACC Card Imaging 2021

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Most patients with MVP and VA have scar, but not all

TABLE 4 Characteristics of Patients With Arrhythmic Events

Case #	Age (yrs)	Sex	MVP	Comorbidity	Mitral RF (%)	LVEF (%)	LVEDV Index (ml/m^2)	Replacement Fibrosis/Pattern	Arrhythmic Events
1	44	Female	Posterior	Dyslipidemia	16	69	84	Yes/patchy	Recurrent syncope with inducible VT/VF
2	73	Male	Bileaflet	None	11	70	61	Yes/patchy	Recurrent syncope with inducible VT
3	80	Female	Posterior	Hypertension, dyslipidemia	37	55	96	Yes/midwall	Sudden cardiac death
4	34	Female	No	None	37	63	62	Yes/patchy	Aborted sudden cardiac arrest
5	41	Male	Bileaflet	None	40	58	124	No	Aborted sudden cardiac arrest
6	65	Male	Posterior	Dyslipidemia	52	77	105	Yes/midwall	Sustained VT
7	28	Female	Bileaflet	None	35	57	102	No	Syncope with documented sustained VT
8	45	Male	Bileaflet	Dyslipidemia	34	58	123	No	Aborted sudden cardiac arrest
9	65	Male	Posterior	Hypertension, dyslipidemia	7	54	53	Yes/midwall	Recurrent syncope with inducible VT

VF = ventricular fibrillation; VT = ventricular tachycardia; other abbreviations as in Table 1.

Autopsy study: 68 consecutive SCD cases with MVP reported as cause of death

- 41% mild MR, mean age 38
- 81% had myocardial fibrosis involving PM and posterior LV

Kitkungvan et al, JACC 2018 *Garbi et al, Open Heart 2018*

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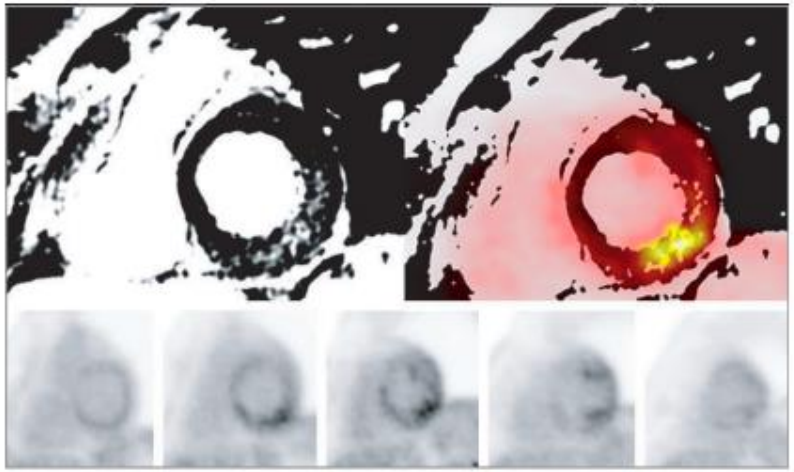
Multimodality approach for evaluation of SCD in MVP

Modality	Parameter	Condition Associated with Increased Risk
ECG/Holter	PVCs	-> Presence of PVCs -> Pap Muscle Origin -> Complex VAs: couplets, triplets, pleo
Echo	Tissue Doppler MAD Strain Mechanical Dispersion	-> Pickelhaube -> longer MAD length -> Impaired global longitudinal strain -> Greater mechanical dispersion
CMR	LGE	-> Presence of replacement fibrosis (LGE) -> Burden of replacement fibrosis? -> Pattern of replacement fibrosis?
PET-MRI		

Subclinical Inflammation contributes to VAs, scar burden and worse outcomes

- PET study: 50% of patients with **unexplained CM and VAs** have evidence of myocardial Inflammation (FDG+)
- PET study: 50% of patients with a **moderte burden of PVCs (>5k)** had evidence of myocardial inflammation (FDG+)
- In some substrates (sarcoid) **combination of inflammation and scar** is especially pro-arrytmic



Miller et al, JAMA Cardiology 2020

Degenerative Mitral Valve Prolapse and Significant Mitral Regurgitation (≥ 3+)
(n= 20)

Hybrid (Simultaneous) PET/MRI

85% PET+ (n=17/20)
70% PET+/MRI+ (n =14/20)

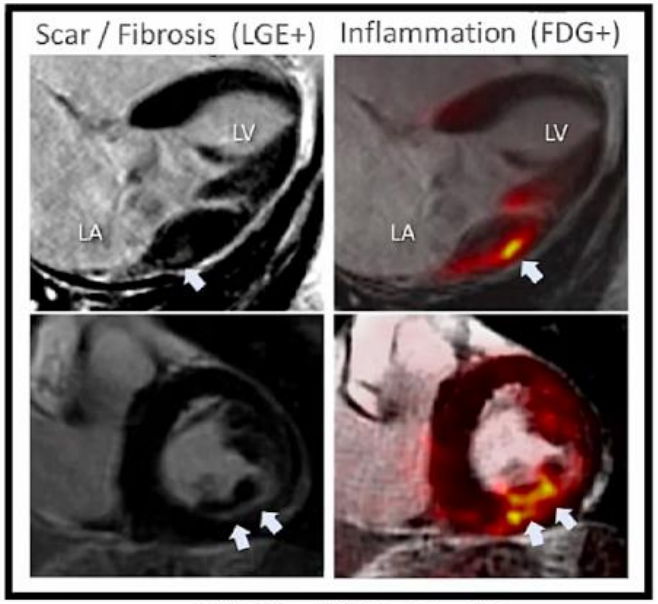
Complex VAs (n=12)

92% PET+ (n=11/12)
67% PET+/MRI+ (n=8/12)

Complex Ventricular Arrhythmias

Late Gadolinium Enhancement: ↑

18F-fluorodeoxyglucose: ↓



Minor VAs (n=8)

75% PET+ (n=6/8)
50% PET+/MRI+ (n=4/8)

Minor Ventricular Arrhythmias

Late Gadolinium Enhancement: ↓

18F-fluorodeoxyglucose: ↑

Miller et al, JAMA Cardiology 2020

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Table. Risk Factors for Sudden Cardiac Death in Mitral Valve Prolapse

Source	Risk factors	MVP, No.	Age, mean (SD), y	Female sex	VT	T-wave inversion	Bileaflet MVP
Nishimura et al,[18] 1985	Leaflet thickness ≥5 mm	237	10-69	60%	NA	NA	NA
Avierinos et al,[29] 2002	Moderate to severe MR; LVEF <50% for increased mortality	833	50 (21)	64%	NA	NA	39%
Carmo et al,[39] 2010	MAD >8.5 mm for NSVT	38	57 (15)	47%	NA	NA	NA
Sriram et al,[17] 2013	Female; VT and bigeminy; higher burden of PVCs (2%) on Holter monitor	10	33 (16)	90%	7 Patients	78%	100%
Basso et al,[30] 2015	LGE fibrosis: SCD—papillary fibrosis in 100% and inferobasal wall in 88%; nonfatal complex VA—93% with LGE on CMR	SCD, 43; living, 44	19-40	SCD, 13%; Living MVP with VA, 70%	30 Patients	78%	70%
Muthukumar et al,[38] 2017	Pickelhaube sign	21	52 (12)	71%	8 Events	50%	100%
Dejgaard, et al,[40] 2018	MAD	MAD, 116; MVP, 90	49 (15)	60%	14 Patients	NA	55 (47%); VT, 5 (36%)
Ermakov et al,[41] 2018	Mechanical dispersion: 59 ms in VA vs 43 ms in no arrhythmia	59	55 (15)	51%	32 Patients	VA, 34%; No VA, 15%	VA, 69%; No VA, 44%

Abbreviations: LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; MAD, mitral annulus disjunction; MR, mitral regurgitation; MVP, mitral valve prolapse; NA, not available; NSVT, nonsustained ventricular tachycardia; PVC, premature ventricular contraction; SCD, sudden cardiac death; VA, ventricular arrhythmia; VT, ventricular tachycardia.

Muthukumar et al, JAMA Cardiology 2020

ESC European Society of Cardiology

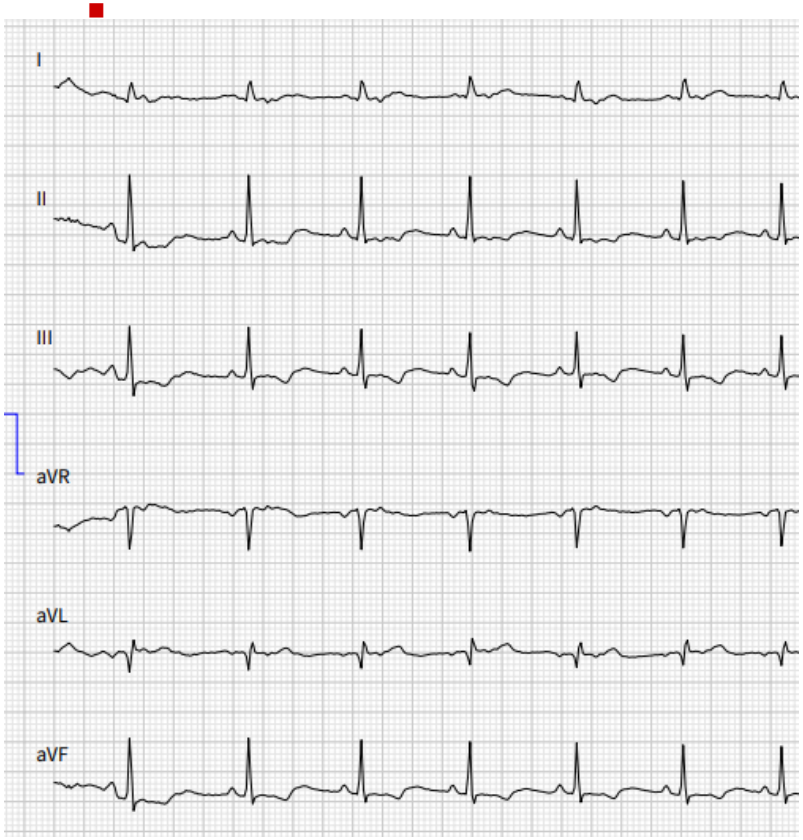
Europace (2022) **00**, 1–23
https://doi.org/10.1093/europace/euac125

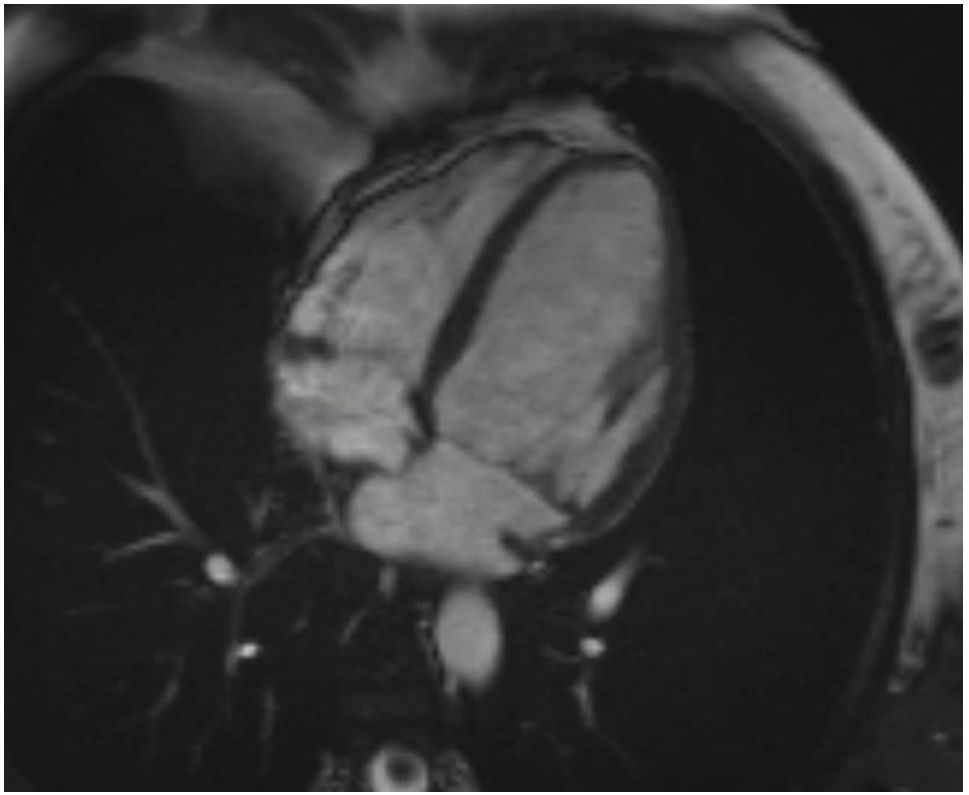
CONSENSUS DOCUMENT

EHRA expert consensus statement on arrhythmic mitral valve prolapse and mitral annular disjunction complex in collaboration with the ESC Council on valvular heart disease and the European Association of Cardiovascular Imaging endorsed cby the Heart Rhythm Society, by the Asia Pacific Heart Rhythm Society, and by the Latin American Heart Rhythm Society

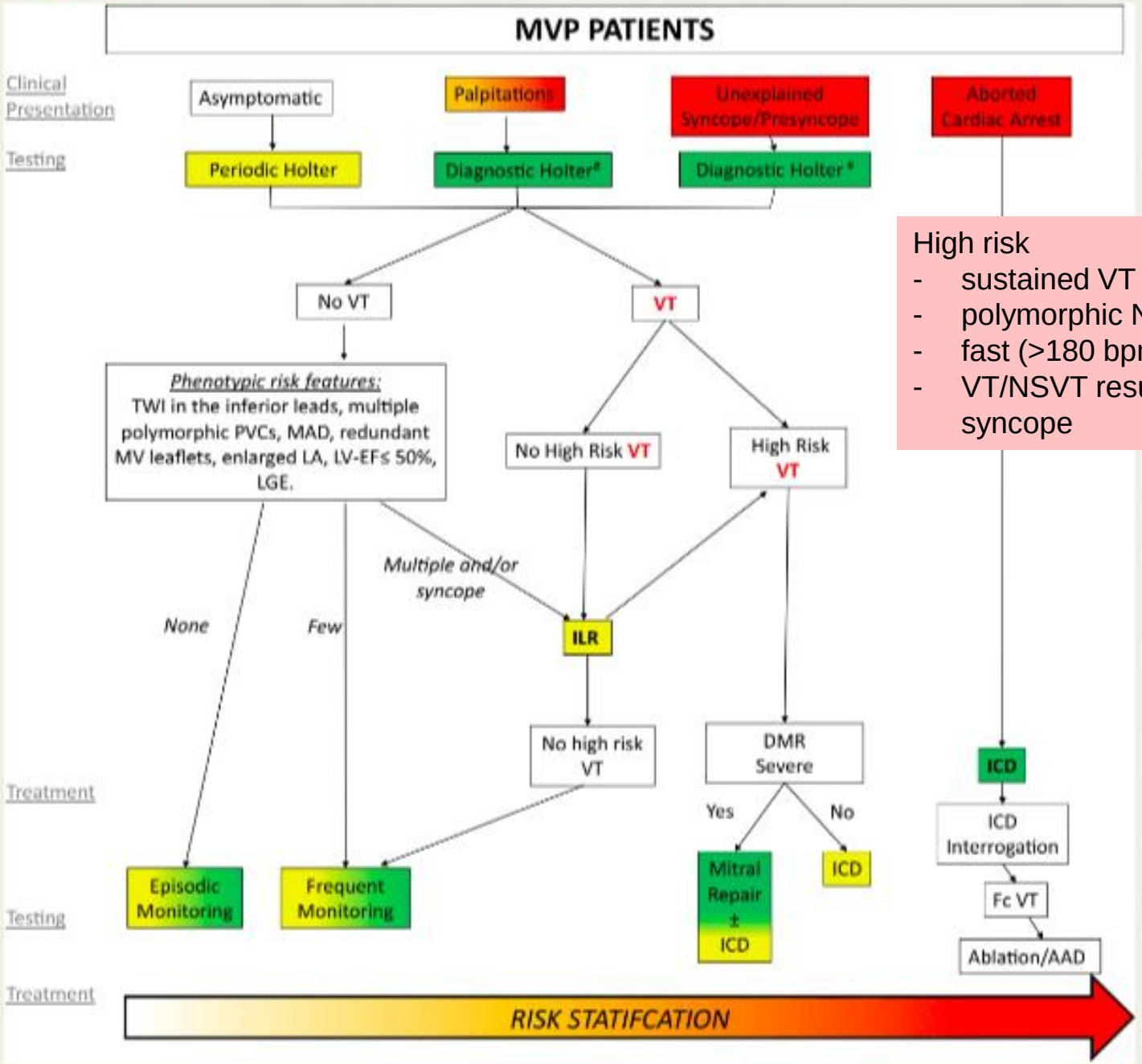
Avi Sabbag (chair) [1]*, Benjamin Essayagh [2,3], Juan David Ramírez Barrera[4], Cristina Basso [5], Ana Berni [6], Bernard Cosyns [7], Jean-Claude Deharo[8], Thomas Deneke [9], Luigi Di Biase[10], Maurice Enriquez-Sarano [11], Erwan Donal [12], Katsuhiko Imai [13], Han S. Lim[14], Nina Ajmone Marsan [15], Mohit K. Turagam[16], Petr Peichl [17], Sunny S. Po[18], and Kristina Hermann Haugaa [19]

Case: 25 yo female with palpitations





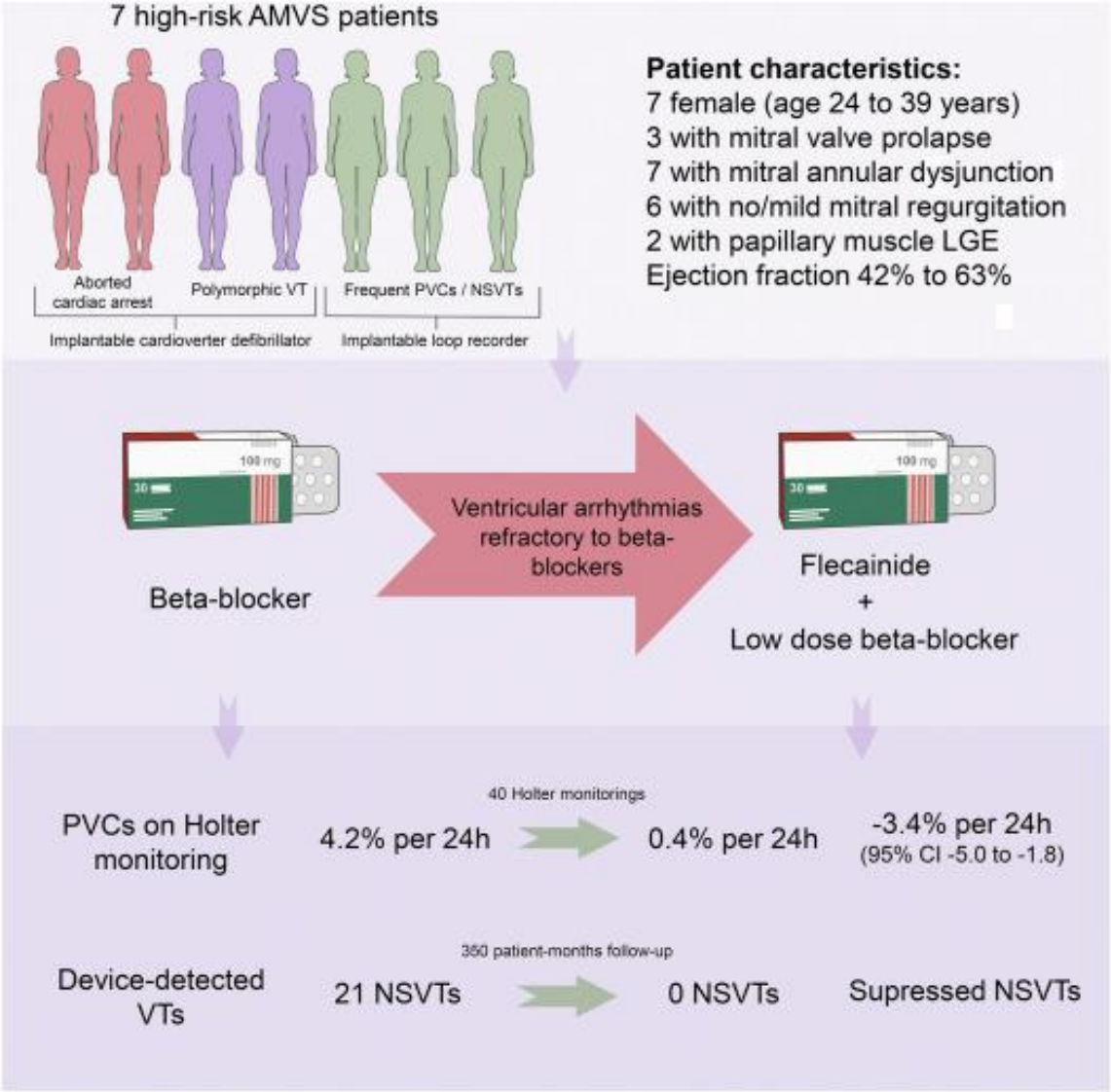
Graphical Abstract



High risk
- sustained VT
- polymorphic NSVT
- fast (>180 bpm) NSVT
- VT/NSVT resulting in syncope

spital

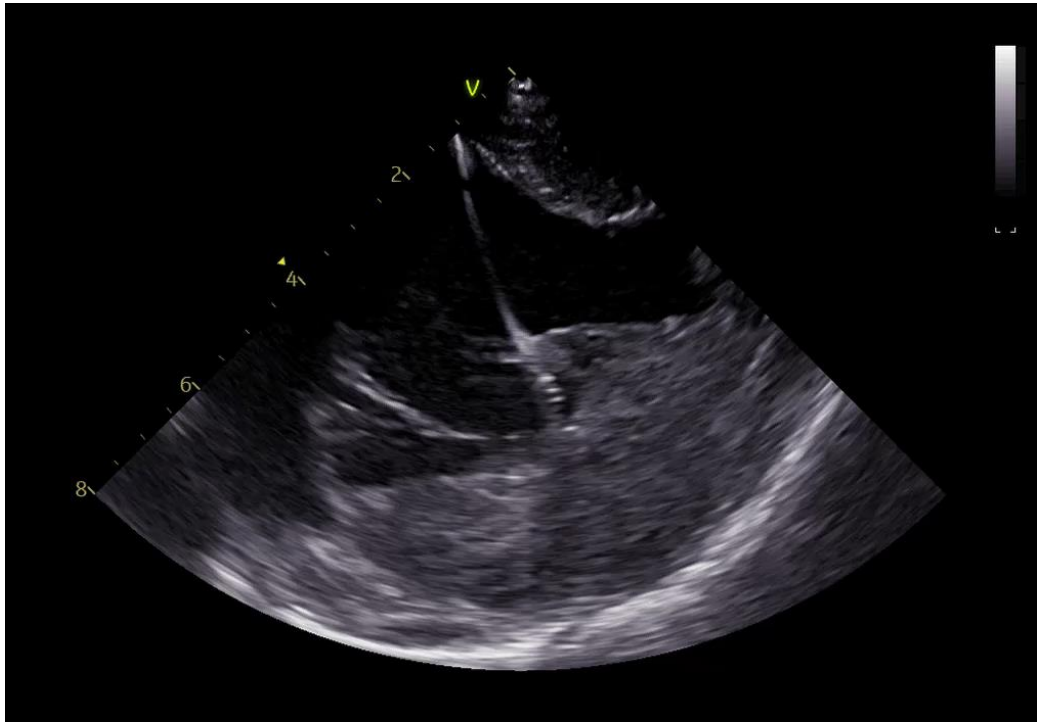
What‘s new?

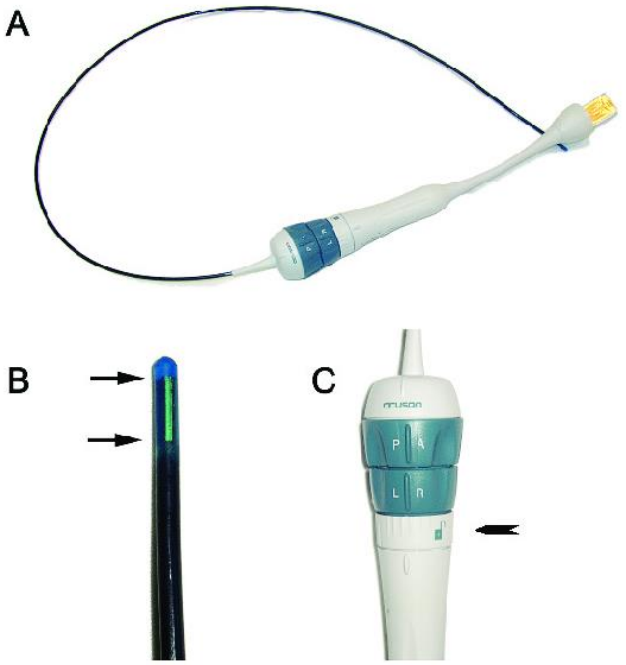


Aabel et al, Heart Rhythm 2022

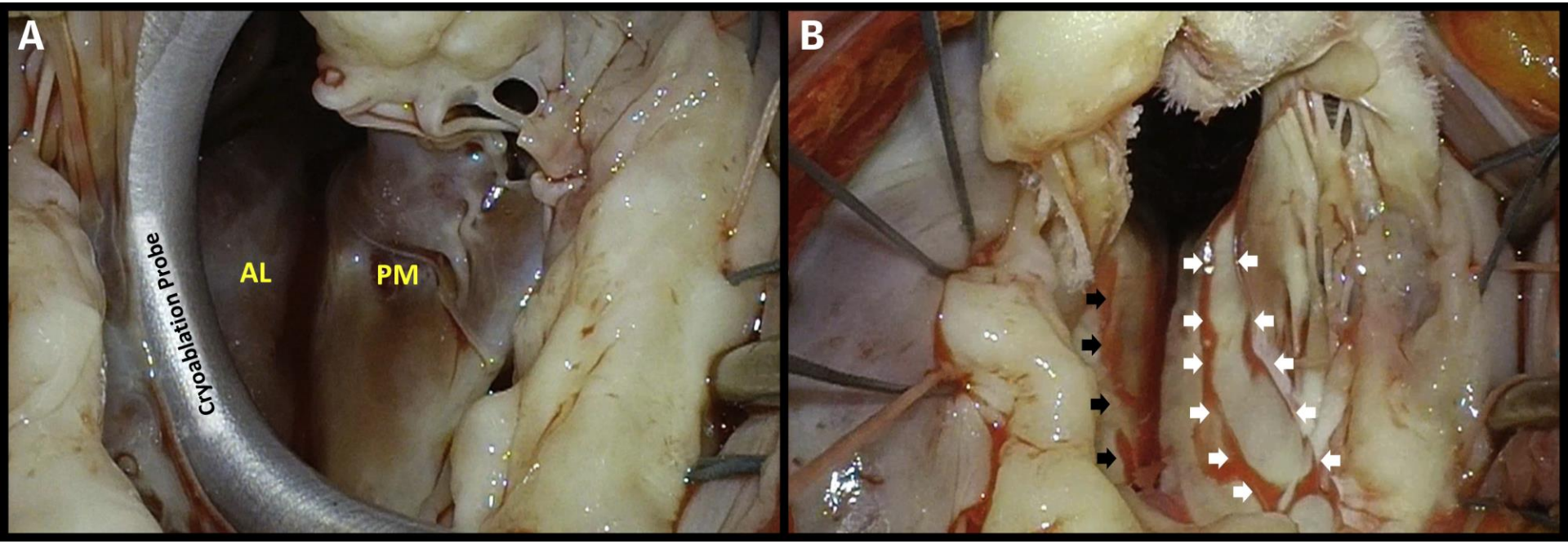
Universitätsspital Basel

Role of catheter ablation?





Role of cardiac surgery?



El-Eshmawi et al, JACC 2022

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Conclusions

- **Replacement fibrosis** is a risk factor for sustained VAs/SCD in MVP and is present in the majority of patients who experience major VAs, but is also present in many patients who never experience any arrhythmic complications.
- **Strain imaging** (GLS and MD) may further enhance our ability to risk stratifiy patients with MVP who are at risk for sustained VA.
- Define tresholds of **LGE and FDG** that are associated with high-risk for SCD in MVP
- **Longitudinal studies** are needed to determine the predictive value of all the currently available risk stratification tools.
- More phenotype and outcomes data are needed

Vielen Dank für Ihre Aufmerksamkeit.

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