Calling for Nominations - *By Oct. 30*

BENTDAHL DISTINGUISHED SERVICE AWARD

Recognizes contributions to MHIF and accomplishments as an **outstanding leader, mentor, philanthropist, educator or researcher**.

2019 recipient: Dr. Elizabeth Grey

ROBERT G. HAUSER LEADERSHIP AWARD

Recognizes contribution to CVD prevention / treatment, advocacy for patients and profession, **visionary leadership and a strong commitment to excellence**.

2019 recipient: Dr. Kevin Harris

Submit to: jwagner@mhif.org

- **Who** you are nominating.
- For **What** award you want them considered.
- **How** they meet the criteria and **Why** you are nominating them.

MHIF FEATURED STUDY:

Proact Xa

COMING SOON!

EPIC message: *Research MHIF Patient Referral*

CONDITION:	PI:	RESEARCH CONTACT:	SPONSOR:
Anticoagulation therapy with On-X aortic valve	Benjamin Sun, MD	Alyssa Taffe, RN Alyssa.Taffe@allina.com | 612-863-7821	CryoLife Inc.

DESCRIPTION:

A prospective, randomized, active (warfarin) controlled, parallel-arm clinical trial to determine if patients with an On-X aortic valve can be maintained safely and effectively on the factor Xa inhibitor apixaban.

There is an unmet need for an alternative anticoagulant drug (such as apixaban) to use instead of warfarin in participants with an aortic mechanical prosthetic valve. Patients will be randomized 1:1 apixaban versus warfarin 90 days or greater s/p surgery.

CRITERIA LIST/ QUALIFICATIONS:

Inclusion:

1. 18 years or greater
2. Able to receive warfarin with a target INR of 2.0-3.0
3. Implantation of an On-X mechanical valve in the aortic position at least 90 days prior to enrollment

Exclusion:

1. Mechanical valve in any other position other than aortic
2. Any cardiac surgery 90 days prior to enrollment
3. Need to be on aspirin > 100 mg daily or a P2Y12 inhibitor
4. On dialysis or creatinine clearance of < 25 mL/min
5. Stroke within 3 months of enrollment

Providing an alternative to warfarin may lead younger patients to choose a mechanical valve with greater durability and better clinical outcomes.

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Creating a world without heart and vascular disease

Minneapolis Heart Institute | Allina Health Abbott Northwestern Hospital

Mitral valve prolapse – when does it stop being benign?

10/12/2020

Iulia Tulai MD, Cardiology Fellow
Minneapolis Heart Institute

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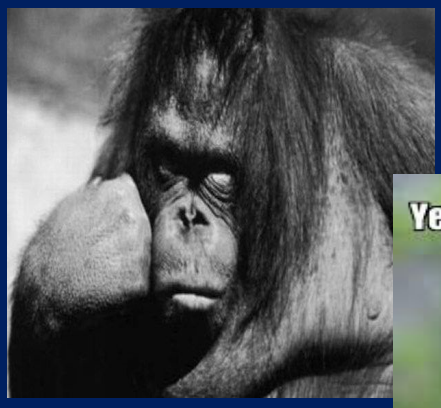
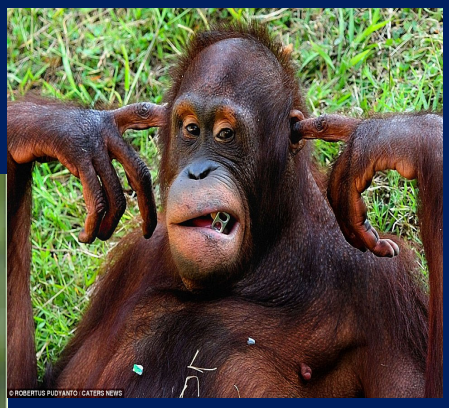
Mitral valve prolapse…





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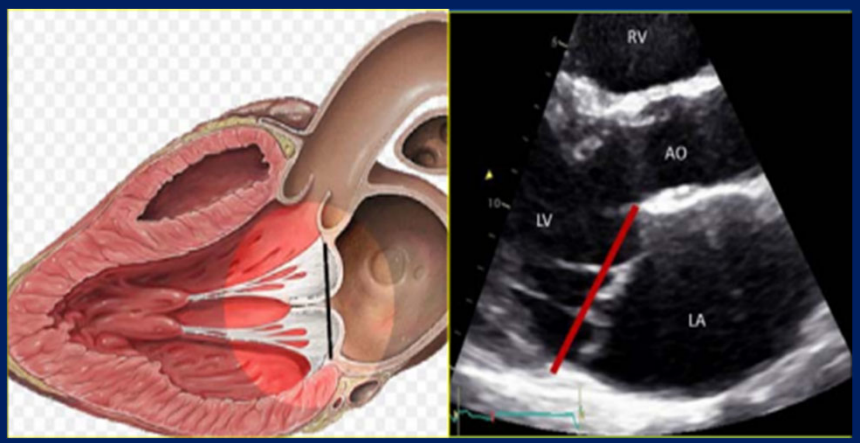
Mitral valve prolapse…

Mitral valve prolapse…

Definition:
- superior displacement of mitral valve leaflet(s) ≥2 mm in systole above the annular plane in PLAX / apical view

- **Classic** (myxomatous degeneration) - thickening of the leaflets ≥5 mm
- **Non-Classic** – thickening of the leaflets <5 mm



1997

Freed et al (Framingham Heart Study, 3,941 participants) – MVP prevalence 2.4%

2020

MVP prevalence in US 2-3%
- 7.8 million individuals in US
- 176 million people world wide

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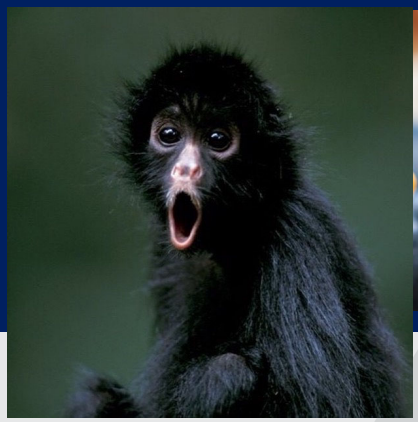
Important / Prognosis?

- Heterogenous prognosis – LVEF, degree of MR, LA enlargement etc.
- One of the less recognized and yet devastating outcomes can be **sudden cardiac death.**



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The prognosis

1966 — MVP first described

1966
1968

Late Systolic Murmurs and Non-Ejection ("Mid-Late") Systolic Clicks
An Analysis of 90 Patients
J. B. BARLOW, C. K. BOSMAN, W. A. POCOCK, AND P. MARCHAND

The syndrome associated with midsystolic click and late systolic murmur
E.W. Hancock M.D.[1], Keith Cohn M.D.[1]

- Malignant arrhythmic MVP entity
- Prevalence / characteristic not fully defined

Benign condition…

1985 — The NEW ENGLAND JOURNAL of MEDICINE

Echocardiographically Documented Mitral-Valve Prolapse — Long-Term Follow-up of 237 Patients
Rick A. Nishimura, M.D., Michael D. McGoon, M.D., Clarence Shub, M.D., Fletcher A. Miller, Jr., M.D., Duane M. Ilstrup, M.S., and A. Jamil Tajik, M.D.

- subsets of MVP patients at high risk development of MR, cerebral embolic events, IE and…

  SCD – **0.4%/year** (6 years follow up)

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The prognosis

2010s

Benign condition???

The Mitral Annulus Disjunction Arrhythmic Syndrome

Arrhythmic Mitral Valve Prolapse: JACC Review Topic of the Week

Bileaflet Mitral Valve Prolapse and Risk of Ventricular Dysrhythmias and Death

Malignant bileaflet mitral valve prolapse syndrome in patients with otherwise idiopathic out-of-hospital cardiac arrest

Natural History of Asymptomatic Mitral Valve Prolapse in the Community

Diffuse myocardial fibrosis in patients with mitral valve prolapse and ventricular arrhythmia

BILEAFLET MITRAL VALVE PROLAPSE AND THE RISK OF VE… DYSRHYTHMIAS AND DEATH

Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death

Mitral Valve Prolapse

Reduction in malignant ventricular arrhythmia and appropriate shocks following surgical correction of bileaflet mitral valve prolapse

Predictors of ventricular arrhythmias in patients with mitral valve

Morphofunctional Abn… Arrhythmic Mitral Valve P…

Familial Clustering of Mitral Valve Prolaps… Community

…ath: A Systematic R…

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SCD incidence

2010s

Reported incidence of SCD varied on:

- methods of evaluation: autopsy vs survival
- study population
- available clinical information
- forensic analysis performed

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SCD incidence

2010s

Reported incidence of SCD varied on:

- methods of evaluation: autopsy vs survival

  ex: autopsy - rarely "unequivocally related"
- study population
- available clinical information
- forensic analysis performed

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SCD incidence

2010s

- 0.2 – 0.4% (Nishimura, NEJM 1985)
- 2% - 4% (athletes) (Narayan, Heart Rhythm 2016 & Finocchiaro JAMA Cardiol 2016)
- 0.14% (Nalliah, Heart 2019)

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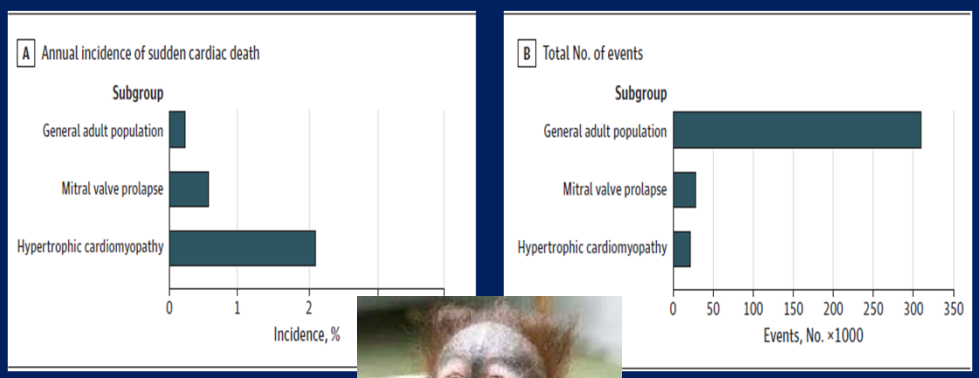
SCD incidence

2020

Figure 1. Estimated Contribution of Mitral Valve Prolapse and Hypertrophic Cardiomyopathy to the Clinical Epidemiology of Sudden Cardiac Death in the United States vs Worldwide



- JAMA Cardiology – Ass , Muthukumar 2020

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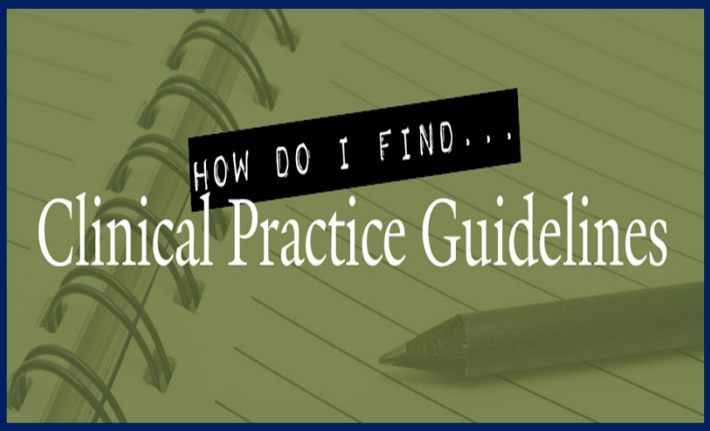
The problem

- **AHA / ESC guidelines** - no specific recommendations yet on identification and risk stratification of SCD in MVP



The problem

How can we identify the **high-risk patient** from a large population of low-risk patients?

Studies on MVP and SCD

TABLE 1 Select Studies of MVP and Sudden Death

First Author, Year (Ref. #)	Study	Patients With MVP	Age (yrs)*	Women (%)	LVEF (%)*	≥Moderate MR (%)	Biphasic or TWI in Inferior Leads (%)	VAs on ECG/ Holter (%)	
Bui et al., 2017 (29)	Retrospective	41	50	3.0	63 ± 7	N/A	N/A	43.7	Myoca
Perazzolo et al., 2016 (30)	Prospective	52	44	63.0	65	None	N/A	63	Mitral l by
Narayanan et al., 2016 (5)	Prospective	17	60.9 ± 16.4	29.4	54.2 ± 14.7	58.8	N/A	29	Young co
Nordhues et al., 2016 (22)	Retrospective	5,669 (bi-MVP), 5,669 (single MVP)	63.5 ± 16.1	47.0	62.0 ± 7.3	46	N/A	3.7†	Bi-MV sin
Fulton et al., 2018 (26)	Retrospective	15	48.5 ± 14.0	78.5	53 ± 8	6.6	33.3	60	Female mu
Muthukumar et al., 2017 (25)	Retrospective	21	51.6 ± 12.3	71.0	N/A	N/A	38	47.6	Spiked vel
Basso et al., 2015 (6)	Retrospective	43	32	61.0	64	None	83	28	Female mu
Sriram et al., 2013 (15)	Retrospective	10 (bi-MVP)	33 ± 16	90.0	60.5 ± 3.1	50	78	100	Female ves
Turker et al., 2010 (23)	Retrospective	58	33.5 ± 11.2	56.0	69.7 ± 2.7	15.5	N/A	34	Moder
Chesler et al., 1983 (34)	Retrospective	14	27 ± 11	86.0	N/A	N/A	14‡	42.8	Endoc

*Median or mean ± SD. †Only ventricular tachycardia (VT) or ventricular fibrillation or SCA. ‡ST-T changes in inferior leads.
bi-MVP = bileaflet mitral valve prolapse; CMR = cardiac magnetic resonance; ECG = electrocardiogram; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; MVP = mitral valve prolapse; N/A = not available; SCA = sudden cardiac arrest; TWI = T-wave inversion; VA = ventricular arrhythmia.

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, Association Between Malignant Mitral Valve prolapse and Sudden Cardiac Death, JAMA Cardiology May 2020

*Miller M et al, Arrhythmic Mitral Valve Prolapse, JACC 2018, 73; 2904-14

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1. Patient characteristics

1) Physical exam
2) Sex
3) Age

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1. Patient characteristics

1) Physical exam
2) Sex
3) Age

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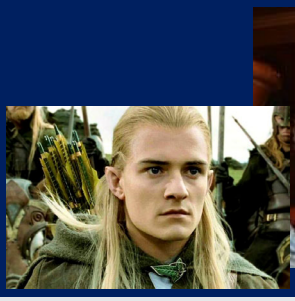
1. Patient characteristics - 1) Physical exam

- For arrhythmic MVP (AMVP), there are no specific physical findings…



Williams syndrome

- Clinical Presentation:
  - Distinctive "elfin" facies
  - mental retardation
  - well-developed verbal skills
  - cheerful disposition, extreme friendliness with strangers
  - cardiovascular problems

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1. Patient characteristics

1) Physical exam ✗
2) Sex
3) Age

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1. Patient characteristics

1) Physical exam ✗
2) Sex
3) Age

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1. Patient characteristics - 2) Sex

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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 May 2020

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1. Patient characteristics - 2) Sex

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Bui et al., 2017 (29)	Retrospective	41	50	3.0	63 ± 7	N/A	N/A	43.7	Myocardial fibrosis by CMR
Perazzolo et al., 2016 (30)	Prospective	52	44	63.0	65	None	N/A	63	Mitral annular disjunction by CMR, mid-systolic click
Narayanan et al., 2016 (5)	Prospective	17	60.9 ± 16.4	29.4	54.2 ± 14.7	58.8	N/A	29	Young age, fewer comorbid conditions
Nordhues et al., 2016 (22)	Retrospective	5,669 (bi-MVP), 5,669 (single MVP)	63.5 ± 16.1	47.0	62.0 ± 7.3	46	N/A	3.7†	Bi-MVP more VT than with single-leaflet MVP
Fulton et al., 2018 (26)	Retrospective	15	48.5 ± 14	78.5	53 ± 8	6.6	33.3	60	Female, bi-MVP and papillary muscle fibrosis by CMR
Muthukumar et al., 2017 (25)	Retrospective	21	51.6 ± 16.8	71.0	N/A	N/A	38	47.6	Spiked systolic lateral mitral annular velocities—Pickelhaube sign
Basso et al., 2015 (6)	Retrospective	43	32	61.0	64	None	83	28	Female and papillary muscles LGE on CMR
Sriram et al., 2013 (15)	Retrospective	10 (bi-MVP)	33 ± 16	90.0	60.5 ± 3.1	50	78	100	Female, inferolateral TWI, complex ventricular ectopy, and bi-MVP
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*Miller M et al, Arrhythmic Mitral Valve Prolapse, JACC 2018

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1. Patient characteristics - 2) Sex

TABLE 1 Baseline Characteristics

	Overall Population (N = 595)	No Arrhythmia (n = 338)	Ventricular Arrhythmia (n = 257)	p Value
Clinical characteristics				
Age, yrs	65 ± 16	63 ± 17	68 ± 15	0.0001
Female	278 (47)	178 (53)	100 (39)	0.0008
BMI, kg/m^2	25 ± 5	25 ± 5	26 ± 5	0.0008
HR, beats/min	68 ± 14	67 ± 14	68 ± 15	0.40
Atrial fibrillation	107 (18)	53 (16)	54 (21)	0.09
Hypertension	227 (38)	119 (35)	108 (42)	0.09
Diabetes	43 (7)	23 (7)	20 (8)	0.60
Dyslipidemia	242 (41)	133 (39)	109 (42)	0.50
CAD history	135 (23)	65 (19)	70 (27)	0.02
Congestive heart failure history	46 (8)	19 (6)	27 (11)	0.03
Charlson Index	0.84 ± 1.10	0.78 ± 1.06	0.92 ± 1.14	0.10
Symptoms				
Syncope history	66 (11)	43 (13)	23 (9)	0.10
Chest pain	110 (18)	69 (20)	41 (16)	0.20
Palpitation	213 (36)	122 (36)	91 (35)	0.90
Dyspnea	210 (35)	114 (34)	96 (37)	0.40
Edema	53 (9)	28 (8)	25 (10)	0.50

Essayagh, Enriquez-Sarano et al, Presentation and Outcome of Arrhythmic Mitral Valve Prolapse, JACC 2020, 76; 637-49

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1. Patient characteristics

1) Physical exam ✗

2) Sex - Male ? ✗

3) Age

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1. Patient characteristics

1) Physical exam ✗

2) Sex - Male ? ✗

3) Age

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1. Patient characteristics - 3) Age

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Muthukumar et al, JAMA Cardiology May 2020

1. Patient characteristics

1) Physical exam ✗
2) Sex - Male ? ✗
3) Age ✗

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2. EKG

- 1) Repolarization abnormalities
- 2) Ventricular arrhythmias (VAs)

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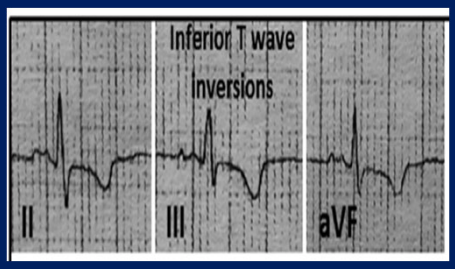
2. EKG

- 1) Repolarization abnormalities
- 2) Ventricular arrhythmias (VAs)

2. EKG – repolarization abnormalities



Miller et al, MVP and Sudden Cardiac Death – JACC 2018

- Abnormal contractility /tugging in MVP
- Regional ischemia

2. EKG – repolarization abnormalities

Table 1. Clinical and Pathological Features of 43 Patients Who Died Suddenly With Isolated MVP

Variables	SCD Resulting From MVP (n=43)	Control Subjects (n=15)	*P* Value
12-Lead ECG available, n (%)	12 (28)	5 (33)	...
Inverted/biphasic T-wave D2, D3, aVF, n (%)	10 (83)	0	...

Basso / Perazzolo et al, Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death, Circulation 2015, 132:556-566

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2. EKG – 1) Repolarization abnormalities

Table 1 Demographics of OHCA Cohort (n = 24)

Demographic	OHCA Cohort	Bileaflet MVP	No MVP	p Value*
n	24/1,200 (2%)‖	10/24 (42%)	14/24 (58%)	—
ST-T repolarization changes#	16/23 (70%)	8/9 (89%)	8/14 (57%)	0.17‡
Inverted/biphasic T wave	12/23 (52%)	7/9 (78%)	4/14 (29%)	0.04‡

Sriram et al, Malignant Bileaflet Mitral Valve Prolapse Syndrome in Patients with otherwise Idiopathic out-of-hospital Cardiac Arrest, JACC 2013, 62:222-30

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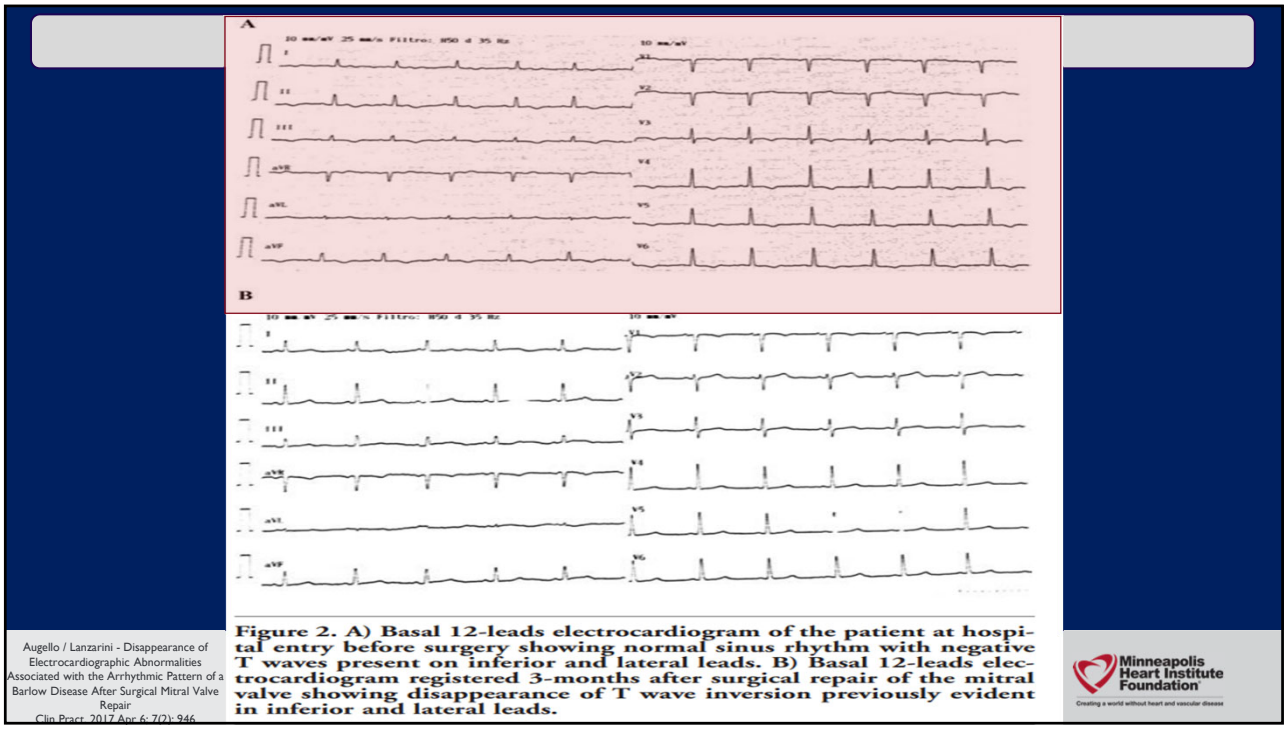

Figure 2. A) Basal 12-leads electrocardiogram of the patient at hospital entry before surgery showing normal sinus rhythm with negative T waves present on inferior and lateral leads. B) Basal 12-leads electrocardiogram registered 3-months after surgical repair of the mitral valve showing disappearance of T wave inversion previously evident in inferior and lateral leads.

Augello / Lanzarini - Disappearance of Electrocardiographic Abnormalities Associated with the Arrhythmic Pattern of a Barlow Disease After Surgical Mitral Valve Repair
Clin Pract. 2017 Apr 6; 7(2): 946

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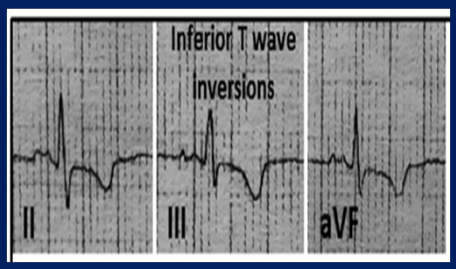
2. EKG – 1) Repolarization abnormalities



Miller et al, MVP and Sudden Cardiac Death – JACC 2018

- In up to 40% of patients with MVP without SCD / sustained VAs
- **33-80%** of patients with MVP-related SCD have biphasic / inverted T waves in inferior leads
- Abnormal T waves in inferior leads is ***not*** risk factor by itself, but risk profile should be further investigated

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2. EKG

- 1) Repolarization abnormalities ?
- 2) Ventricular arrhythmias (VAs)

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2. EKG

- 1) Repolarization abnormalities
- 2) Ventricular arrhythmias (VAs)

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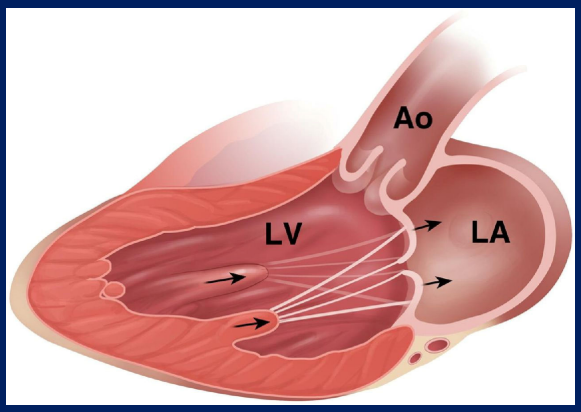
2. EKG

LABORATORY INVESTIGATION
ELECTROPHYSIOLOGY

Electrophysiologic effects of papillary muscle traction in the intact heart

CHARLES C. GORNICK, M.D., H. GARETH TOBLER, M.D., MARC C. PRITZKER, M.D., ISHIK C. TUNA, M.D., ADRIAN ALMQUIST, M.D., AND DAVID G. BENDITT, M.D.

Circulation 73, No. 5, 1013–1021, 1986.



Mitral valve prolapse - JACC Imaging, 2008

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IT1

2. EKG

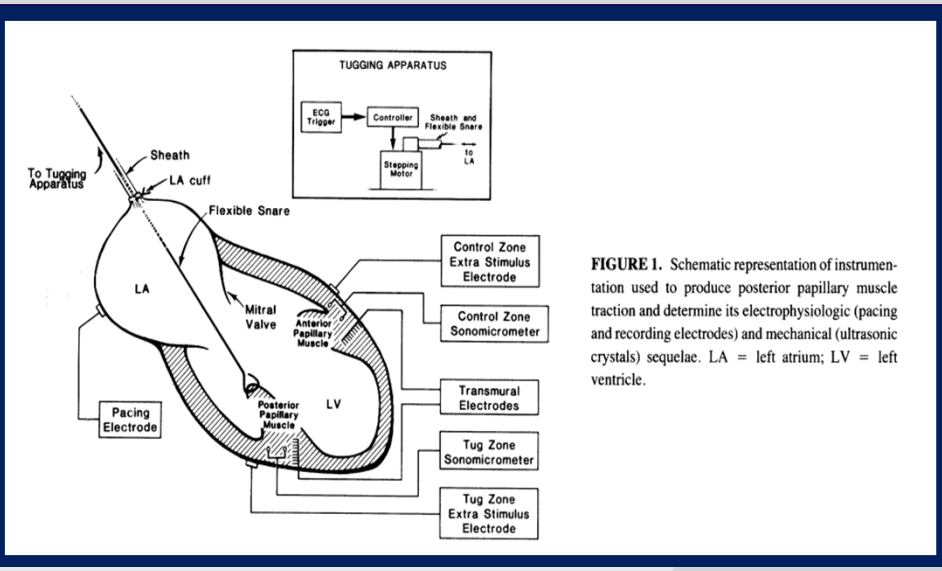

FIGURE 1. Schematic representation of instrumentation used to produce posterior papillary muscle traction and determine its electrophysiologic (pacing and recording electrodes) and mechanical (ultrasonic crystals) sequelae. LA = left atrium; LV = left ventricle.

Gornick et al Electrophysiologic effects of papillary muscle traction in the intact heart
Circulation 73, No. 5, 1013-1021, 1986.

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Slide 38

IT1 Iulia-Maria Tulai, 10/10/2020

2. EKG

- *"In normal myocardium in situ, regional abnormal wall motion may be associated with alterations of local ventricular activation and refractoriness, factors that in the diseased heart may lead to increased susceptibility to arrhythmias"*

Electrophysiologic effects of papillary muscle traction in the intact heart

Charles C. Gornick, M.D., H. Gareth Tobler, M.D., Marc C. Pritzker, M.D., Ishik C. Tuna, M.D., Adrian Almquist, M.D., and David G. Benditt, M.D.

Circulation 73, No. 5, 1013–1021, 1986.

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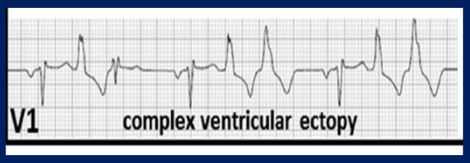
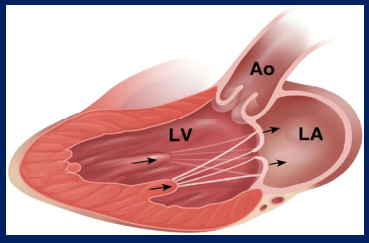
2. EKG – 2) VAs

- PVCs - Common in MVP, with or without SCD (~40-50%)
- Frequently from papillary muscle region and outflow tract
  - Regional stretch? Abnormal Ca++ handling?
- PVCs (isolated / complex)
  - Not enough by themselves to deem high risk
  - Consider additional risk stratification



Miller et al, MVP and Sudden Cardiac Death – JACC 2018



Mitral valve prolapse - JACC Imaging, 2008

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2. EKG – 2) VAs

- PVCs **origin** - marker of SCD?
- In patients with BiMVP and SCD, Purkinje system plays a central role in arrhythmogenesis
- Ablation of clinically dominant VE foci
  - improved symptoms
  - reduced appropriate ICD shocks

Sites of Successful Ventricular Fibrillation Ablation in Bileaflet Mitral Valve Prolapse Syndrome

Faisal F. Syed, MBChB; Michael J. Ackerman, MD, PhD; Christopher J. McLeod, MD, PhD; Suraj Kapa, MD; Siva K. Mulpuru, MBBS; Chenni S. Sriram, MD; Bryan C. Cannon, MD; Samuel J. Asirvatham, MD; Peter A. Noseworthy, MD

Table 2. Localization of Dominant Ventricular Ectopy in Cardiac Arrest and Nonarrest Patients

	Cardiac Arrest (n=6)	Nonarrest (n=8)
No. of ventricular ablation procedures (total [limits per patient])	8 (limits 1–2)	11 (1–2)*
Ablation period	11/2010 to 3/2015	2/2007 to 9/2013
Anatomic location of dominant VE		
LV papillary muscle	4/6†	5/8‡
LV fascicle (nonpapillary)	4/6†	4/8‡
RVOT	0	1
Purkinje target	6/6	5/8
Location of Purkinje target		
LV papillary muscle	4/6§	3/8‖
LV fascicle (nonpapillary)	4/6§	5/8‖
Ablation-induced VF from target VE	4/6	2/8

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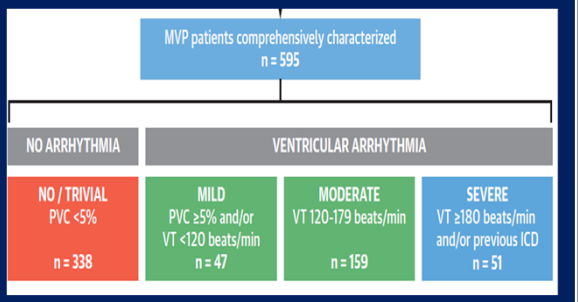
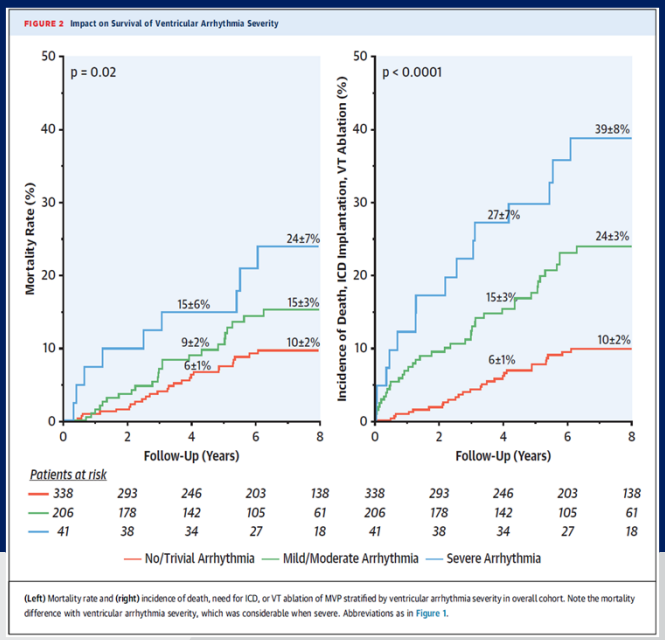
2. EKG – 2) VAs

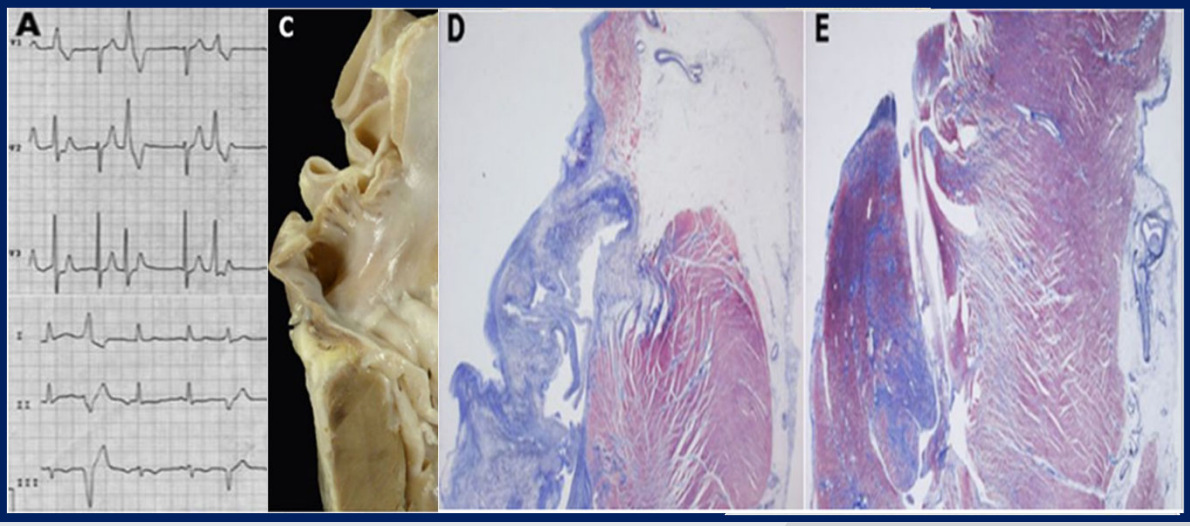


Essayagh / Enriquez-Sarano et al, Presentation and Outcome of Arrhythmic Mitral Valve Prolapse, JACC 2020;76:637–49



(Left) Mortality rate and (right) incidence of death, need for ICD, or VT ablation of MVP stratified by ventricular arrhythmia severity in overall cohort. Note the mortality difference with ventricular arrhythmia severity, which was considerable when severe. Abbreviations as in Figure 1.

2. EKG



Basso / Perazzolo et al, Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death, Circulation 2015, 132:556-566

2. EKG

- 1) Repolarization abnormalities ?
- 2) Ventricular arrhythmias (VAs) ✓

3. Echocardiographic findings

- 1) Leaflet characteristics
- 2) Mitral regurgitation
- 3) Lateral mitral annular velocities
- 4) Mitral annular disjunction (MAD)
- 5) Speckle-Tracking Doppler

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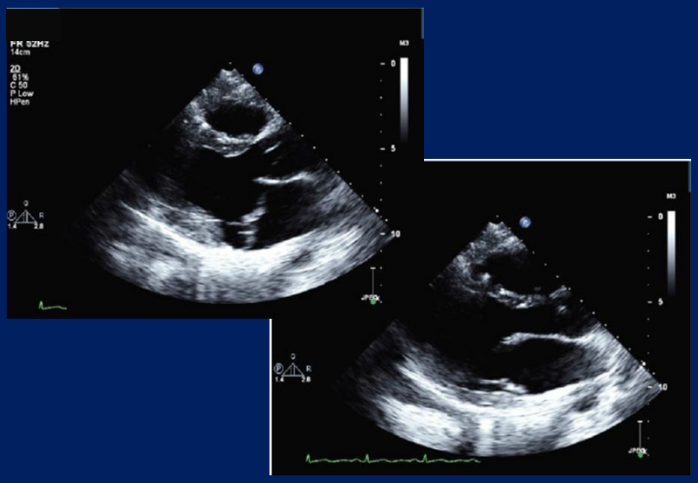
3. Echo findings – 1) Leaflet characteristics

A. Bileaflet MVP (BiMVP)



Sriram et al, Malignant Bileaflet Mitral Valve Prolapse Syndrome in Patients with otherwise Idiopathic out-of-hospital Cardiac Arrest, JACC 2013, 62:222-30

3. Echo findings – 1) Leaflet characteristics

A. Bileaflet MVP (BiMVP)

- Proposed as high risk feature for SCD
- 42% out of 24 young patients with idiopathic SCD had BiMVP

Table 1 Demographics of OHCA Cohort (n = 24)

Demographic	OHCA Cohort	Bileaflet MVP	No MVP	p Value*
n	24/1,200 (2%)‖	10/24 (42%)	14/24 (58%)	—
Age at sentinel event (yrs)	32 ± 15 (median 33.5; range: 5-60)	33 ± 16 (median 34.7; range: 5-60)	32 ± 14 (median 29.4; range: 14-51)	0.84†
Women	16 (67%)	9/10 (90%)	7/14 (50%)	0.04

Sriram et al, Malignant Bileaflet Mitral Valve Prolapse Syndrome in Patients with otherwise Idiopathic out-of-hospital Cardiac Arrest, JACC 2013, 62:222-30

3. Echo findings – 1) Leaflet characteristics

A. Bileaflet MVP (BiMVP)

- Proposed as high risk feature for SCD

TABLE 1 Select Studies of MVP and Sudden Death

First Author, Year (Ref. #)	Study	Patients With MVP	Age (yrs)*	Women (%)	LVEF (%)*	≥Moderate MR (%)	Biphasic or TWI in Inferior Leads (%)	VAs on ECG/ Holter (%)	Comments
Bui et al., 2017 (29)	Retrospective	41	50	3.0	63 ± 7	N/A	N/A	43.7	Myocardial fibrosis by CMR
Perazzolo et al., 2016 (30)	Prospective	52	44	63.0	65	None	N/A	63	Mitral annular disjunction by CMR, mid-systolic click
Narayanan et al., 2016 (5)	Prospective	17	60.9 ± 16.4	29.4	54.2 ± 14.7	58.8	N/A	29	Young age, fewer comorbid conditions
Nordhues et al., 2016 (22)	Retrospective	5,669 (bi-MVP), 5,669 (single MVP)	63.5 ± 16.1	47.0	62.0 ± 7.3	46	N/A	3.7†	Bi-MVP more VT than with single-leaflet MVP
Fulton et al., 2018 (26)	Retrospective	15	48.5 ± 14.0	78.5	53 ± 8	6.6	33.3	60	Female, bi-MVP and papillary muscle fibrosis by CMR
Muthukumar et al., 2017 (25)	Retrospective	21	51.6 ± 12.3	71.0	N/A	N/A	38	47.6	Spiked systolic lateral mitral annular velocities—Pickelhaube sign
Basso et al., 2015 (6)	Retrospective	43	32	61.0	64	None	83	28	Female and papillary muscles LGE on CMR
Sriram et al., 2013 (15)	Retrospective	10 (bi-MVP)	33 ± 16	90.0	60.5 ± 3.1	50	78	100	Female, inferolateral TWI, complex ventricular ectopy, and bi-MVP
Turker et al., 2010 (23)	Retrospective	58	33.5 ± 11.2	56.0	69.7 ± 2.7	15.5	N/A	34	Moderate-severe MR
Chesler et al., 1983 (34)	Retrospective	14	27 ± 11	86.0	N/A	N/A	14‡	42.8	Endocardial friction lesions

*Median or mean ± SD. †Only ventricular tachycardia (VT) or ventricular fibrillation or SCA. ‡ST-T changes in inferior leads.
bi-MVP = bileaflet mitral valve prolapse; CMR = cardiac magnetic resonance; ECG = electrocardiogram; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; MVP = mitral valve prolapse; N/A = not available; SCA = sudden cardiac arrest; TWI = T-wave inversion; VA = ventricular arrhythmia.

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3. Echo findings – 1) Leaflet characteristics

A. Bileaflet MVP (BiMVP)

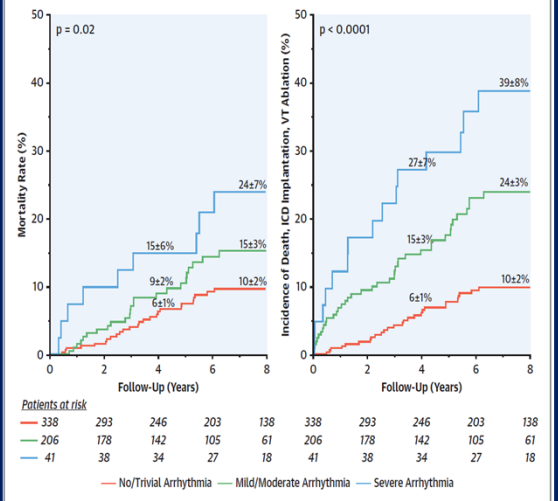
- Essayagh – more VAs in patients with BiMVP compared to SiMVP

TABLE 1 Baseline Characteristics

	Overall Population (N = 595)	No Arrhythmia (n = 338)	Ventricular Arrhythmia (n = 257)	p Value
Echocardiographic variables				
Bileaflet	280 (47)	141 (42)	139 (55)	0.003

Essayagh, Enriquez-Sarano et al, Presentation and Outcome of Arrhythmic Mitral Valve Prolapse, JACC 2020, 76; 637-49

FIGURE 2 Impact on Survival of Ventricular Arrhythmia Severity



(Left) Mortality rate and (right) incidence of death, need for ICD, or VT ablation of MVP stratified by ventricular arrhythmia severity in overall cohort. Note the mortality difference with ventricular arrhythmia severity, which was considerable when severe. Abbreviations as in Figure 1.

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3. Echo findings – 1) Leaflet characteristics

A. Bileaflet MVP

- Bileaflet involvement found in 70% of the patients ≤ 40 years old with SCD and MVP

Table 1. Clinical and Pathological Features of 43 Patients Who Died Suddenly With Isolated MVP

Variables	SCD Resulting From MVP (n=43)	Control Subjects (n=15)	*P* Value
MVP leaflet involvement			
Posterior, n (%)	13 (30)	0	...
Bileaflet, n (%)	30 (70)	0	...
Endocardial fibrous plaque, n (%)	25 (58)	0	...

Basso / Perazzolo et al, Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death, Circulation 2015, 132:556-566

3. Echocardiographic findings

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3. Echo findings – 2) MR

Moderate-Severe MR

- Until recently thought to be an independent predictor of SCD (relative risk 8.4) (Turker, 2010)
- Conclusion derived from studies showing MR as independent predictor of complex VAs, not mortality

Predictors of ventricular arrhythmias in patients with mitral valve prolapse.

Turker Y[1], Ozaydin M, Acar G, Ozgul M, Hoscan Y, Varol E, Dogan A, Erdogan D, Yucel H.

Author information

Abstract

Arrhythmias have been reported to occur frequently in symptomatic patients with mitral valve prolapse (MVP). The mechanisms causing ventricular arrhythmias in patients with MVP have not been fully investigated. The purpose of this study was to determine the clinical, echocardiographic and heart rate variability parameters, and plasma concentrations of electrolytes and inflammatory markers in predicting ventricular arrhythmias in patients with MVP. A total of 58 consecutive patients with MVP were included in this study. We performed electrocardiography, echocardiography, holter analysis, routine biochemical tests including plasma concentrations of electrolytes and inflammatory markers, and evaluated the clinical characteristics. Ventricular arrhythmia defined as occurrence of any of the followings: ventricular premature contractions (VPCs), VPC couplets, and ventricular tachycardia documented by holter analysis, continuous monitoring or by electrocardiography. Twenty patients (34%) had ventricular arrhythmias, and 38 (66%) patients had no ventricular arrhythmias. Seventeen patients had VPC, 2 patients had VPC couplets and 1 patient had ventricular tachycardia. Univariable predictors of ventricular arrhythmias included isovolumetric relaxation time and the occurrence of moderate to severe mitral regurgitation. Multivariable logistic regression analysis showed that occurrence of moderate to severe mitral regurgitation was the only independent predictor of ventricular arrhythmias (relative risk: 8.42, 95% confidence interval: 1.49-47.64, p = 0.01). Present study showed that the only independent predictor of ventricular arrhythmias in patients with MVP is the occurrence of moderate to severe mitral regurgitation.

3. Echo findings – 2) MR

- **Dollar - 1991**: 14/15 patients who had MVP-related SCD did not have significant (at least moderate) MR

JACC Vol. 17, No. 4
March 15, 1991:921-31

MORPHOLOGIC STUDIES

Morphologic Comparison of Patients With Mitral Valve Prolapse Who Died Suddenly With Patients Who Died From Severe Valvular Dysfunction or Other Conditions

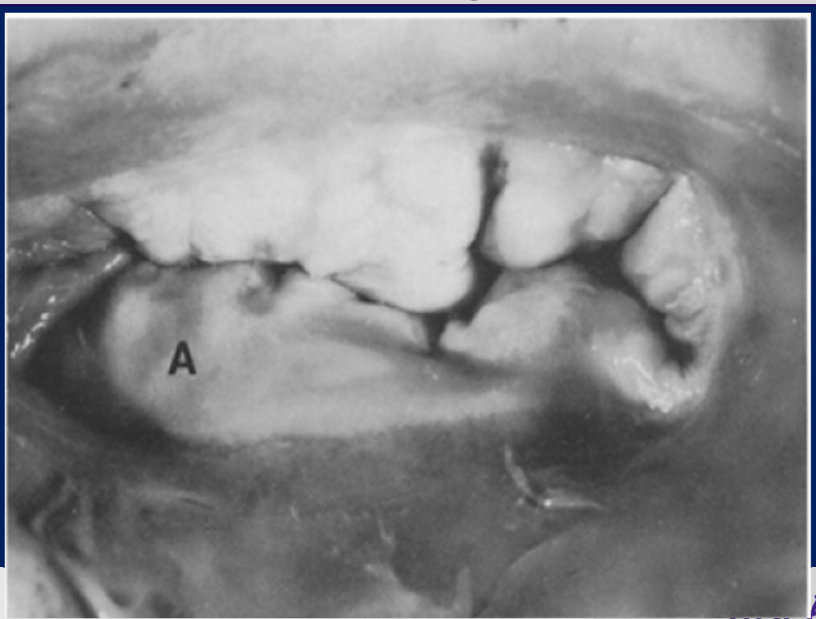
ALLEN L. DOLLAR, MD,* WILLIAM C. ROBERTS, MD, FACC
Bethesda, Maryland

Table 1. Clinical and Morphologic Features of Mitral Valve Prolapse at Necropsy Unassociated With Other Congenital Cardiovascular Anomalies 149 patients aged 16 to 70 years)

Patient Category	+SCD −MR −CAD	+SCD +MR −CAD	+SCD +MR +CAD	−SCD +MR −CAD	−SCD −MR −CAD	Total (%)
No. of patients	14	3	3	10	19	49
SCD due to MVP	14/14	1/3	0/3	0/10	0/19	15/49 (31)

AML = anterior mitral leaflet; CA = coronary artery; CAD = fatal coronary artery disease; CSA = cross-sectional area; FO = fossa ovale; LV = left ventricular; MR = severe mitral regurgitation; MV = mitral valve; MVP = mitral valve prolapse; PFO = patent foramen ovale; PML = posterior mitral leaflet; SCD = sudden cardiac death; TV = tricuspid valve; − = absent; + = present.

3. Echo findings – 2) MR



Dollar et al, Morphologic Comparison of Patients With Mitral Valve Prolapse Who Died Suddenly With Patients Who Died From Severe Valvular Dysfunction or Other Conditions, JACC 1991, 17:921-31

3. Echo findings – 2) MR

- **Essayagh / Enriquez- Sarano, 2020**: 595 consecutive MVP patients: "severe MR was not an independent predictor for VAs"

TABLE 1 Baseline Characteristics

	Overall Population (N = 595)	No Arrhythmia (n = 338)	Ventricular Arrhythmia (n = 257)	p Value
MR				<0.0001
No/trivial	215 (36)	159 (47)	56 (22)	
Mild	47 (8)	25 (7)	22 (9)	
Moderate	167 (28)	79 (23)	88 (34)	
Severe	166 (28)	75 (22)	91 (35)	
ERO, mm^2	15 (0–29)	9 (0–25)	20 (8–34)	<0.0001
RVol, ml	25 (0–50)	14 (0–42)	34 (13–57)	<0.0001

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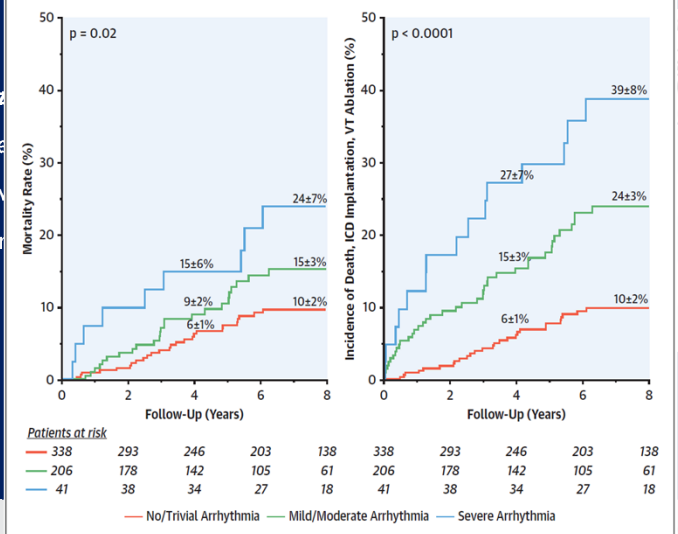
3. Echo findings – 2) MR

- **Essayagh / Enriquez**
- **2020**: 595 consecutive
- patients: "severe MR
- independent predictor

FIGURE 2 Impact on Survival of Ventricular Arrhythmia Severity



(Left) Mortality rate and (right) incidence of death, need for ICD, or VT ablation of MVP stratified by ventricular arrhythmia severity in overall cohort. Note the mortality difference with ventricular arrhythmia severity, which was considerable when severe. Abbreviations as in Figure 1.

ups characteristics overall

arrhythmia (n=257)		
Moderate (n=159)	Severe (n=51)	P value
		<0.0001
36 (23)	12 (24)	
12 (8)	4 (8)	
57 (36)	17 (33)	
54 (34)	18 (35)	

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3. Echocardiographic findings

- 1) Leaflet characteristics – Bileaflet MVP ✓
- 2) Mitral regurgitation – Significant MR ? ✗
- 3) Lateral mitral annular velocities
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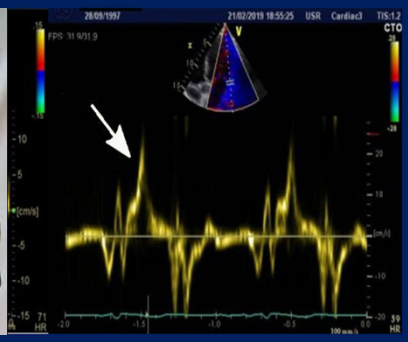
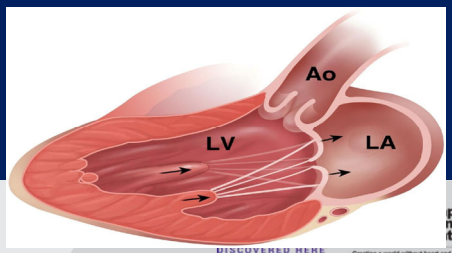
3. Echo findings – Pickelhaube sign

Pickelhaube sign:

- peak systolic mitral annulus velocity ≥16 cm/sec
- Muthukumar et al: - BiMVP
  - Patients with this criteria were more likely to have malignant VAs (67% vs 22%, p<0.08)
  - LGE by MRI was only present in the group with + Pickelhaube sign (33%)
  - Novel echocardiographic risk marker for malignant MVP syndrome - BiMVP





Mitral valve prolapse - JACC Imaging, 2008

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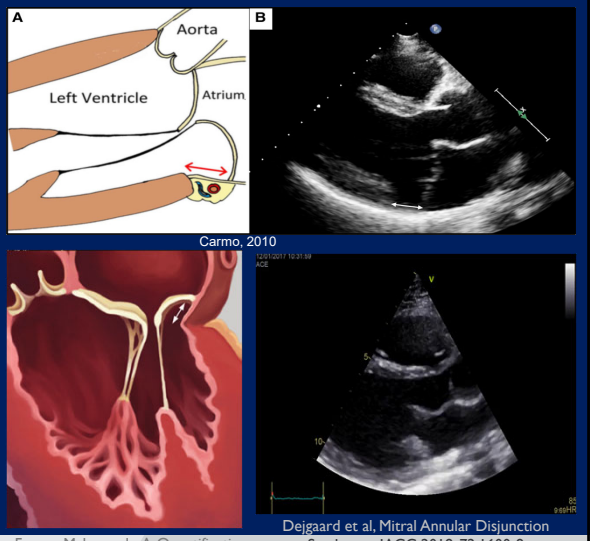
3. Echo findings – 4) MAD

- **Mitral annular disjunction (MAD):**
  - Detachment of the roots of the annulus from the ventricular myocardium to which it would normally be attached
  - Allows for mitral annulus hypermobility



Carmo, 2010

Dejgaard et al, Mitral Annular Disjunction Syndrome, JACC 2018, 72:1600-9

Feroze Mahmood - A Quantification Approach to Echocardiography of Mitral Valve for Repair, 2015, Anesthesia & Analgesia 12(1):34-58

3. Echo findings – 4) MAD

RESEARCH Open Access

Mitral annular disjunction in myxomatous mitral valve disease: a relevant abnormality recognizable by transthoracic echocardiography

Pedro Carmo[1*], Maria J Andrade[1], Carlos Aguiar[1], Rui Rodrigues[2], Raquel Gouveia[1], José A Silva[1]

Carmo, 2010:

- Severity of MAD is associated with VA burden
- A disjunction greater than 8.5 mm was a reasonable criterion to predict the risk of NSVT
  - Sensitivity of 67%
  - Specificity of 83%
  - Odds ratio = 10; 95% CI: 1.28 -78.1

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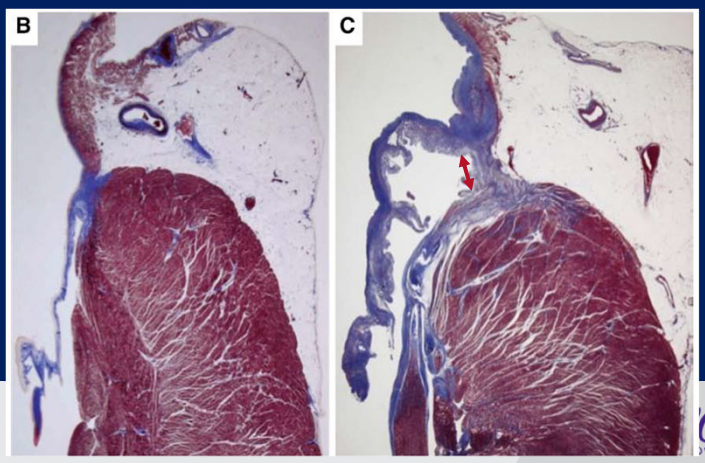
3. Echo findings – 4) MAD

Morphofunctional Abnormalities of Mitral Annulus and Arrhythmic Mitral Valve Prolapse

Martina Perazzolo Marra, Cristina Basso, Manuel De Lazzari, Stefania Rizzo, Alberto Cipriani, Benedetta Giorgi, Carmelo Lacognata, Ilaria Rigato, Federico Migliore, Kalliopi Pilichou, Luisa Cacciavillani, Emanuele Bertaglia, Anna Chiara Frigo, Barbara Bauce, Domenico Corrado, Gaetano Thiene, and Sabino Iliceto

Originally published 11 Aug 2016 | https://doi.org/10.1161/CIRCIMAGING.116.005030 | Circulation: Cardiovascular Imaging. 2016;9



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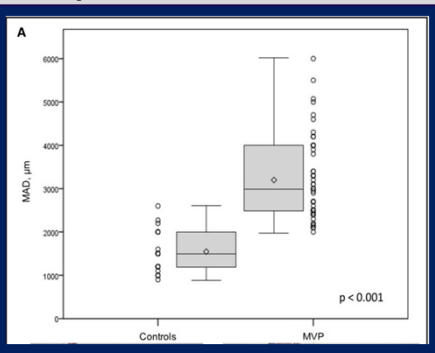
3. Echo findings – 4) MAD

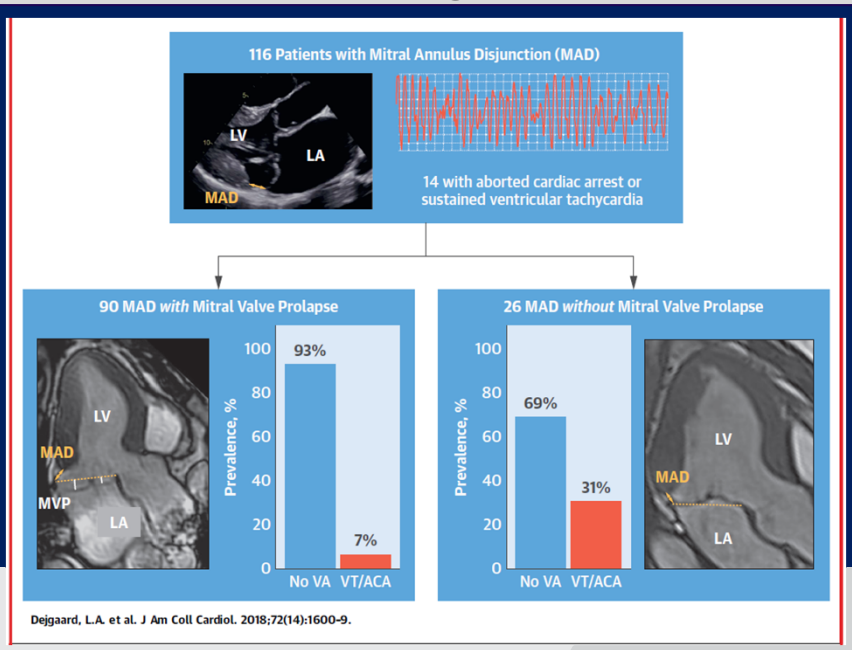
Perazollo, 2016:

- Length of MAD in MVP-SCD patients is significantly higher than in controls
- MAD was significantly longer in patients with LGE on MRI compared to those without LGE on MRI
- MAD = constant feature of arrhythmic MVP with LV fibrosis



Variables	MVP With Midsystolic Click (32 Patients)	MVP Without Midsystolic Click (20 Patients)	*P*
Length of MAD, mm	4.8 (3 to 7)	3 (2.3 to 4.8)	0.089
Curling, n (%)	27 (84)	10 (50)	0.008
Curling, mm	4.8 (1.8 to 5.5)	1.2 (0 to 4)	0.009
Severe curling (≥3.5 mm), n(%)	20 (63)	6 (30)	0.023
LGE, n(%)	26 (81)	10 (50)	0.018

3. Echo findings – 4) MAD



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

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3. Echocardiographic findings

- 1) Leaflet characteristics – Bileaflet MVP ✓
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- 3) Lateral mitral annular velocities - Pickelhaube sign (Bileaflet MVP) ✓
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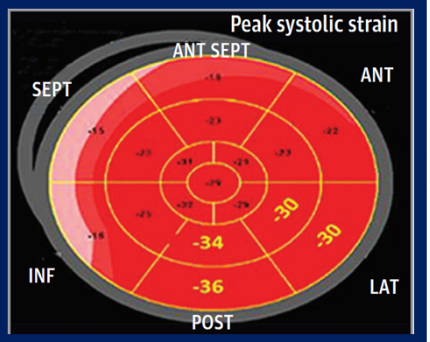
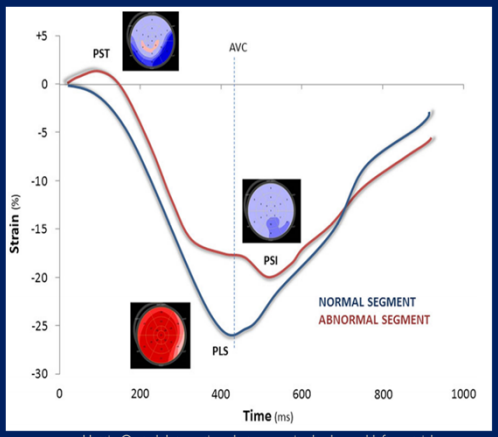
3. Echo findings – 5) Speckle Tracking

- Supranormal strain (>24%) is witnessed in the posterolateral LV trident
- Subnormal strain (<18%) is seen in the corresponding opposite basal septal wall segments
- Postsystolic contraction (postsystolic shortening, incoordinate contraction)



Muthukumar et al, Association Between MVP and SCD, JAMA Cardiology 2020



Huttin O et al, Interactions between mitral valve and left ventricle analyzed by 2D speckle tracking in patients with mitral valve prolapse: one more piece to the puzzle, EHJ CV Imaging 2017

3. Echocardiographic findings

- 1) Leaflet characteristics – Bileaflet MVP ✓
- 2) Mitral regurgitation – Significant MR ? ✗
- 3) Lateral mitral annular velocities - Pickelhaube sign (Bileaflet MVP) ✓
- 4) Mitral annular disjunction (MAD) ✓
- 5) Speckle-Tracking Doppler ✓

4. MRI findings

- 1) MAD
- 2) Curling
- 3) Fibrosis

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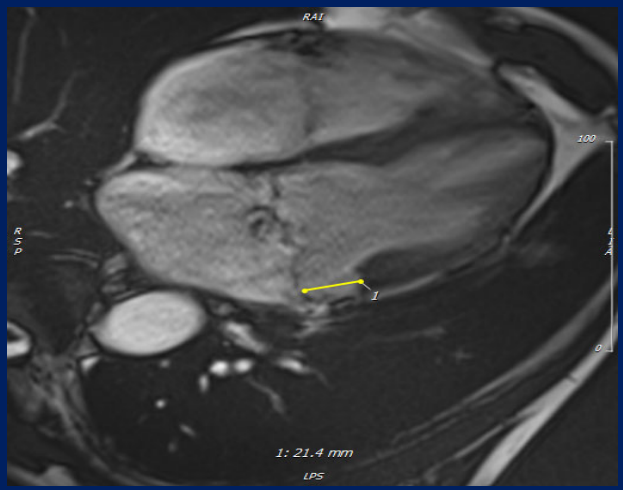
4. MRI findings

- 1) MAD ✓
- 2) Curling
- 3) Fibrosis



Cardiac MRI, steady state free precession (SSFP) sequence demonstrates mitral annular disjunction (yellow line). This was measured at 2.1 cm.

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4. MRI findings

- 1) MAD
- 2) Curling
- 3) Fibrosis

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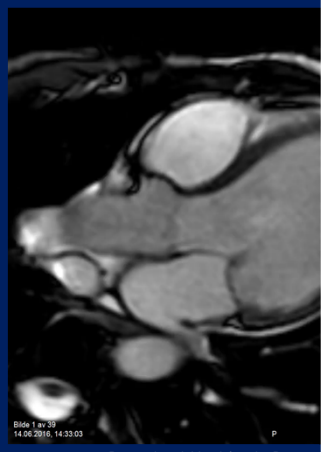
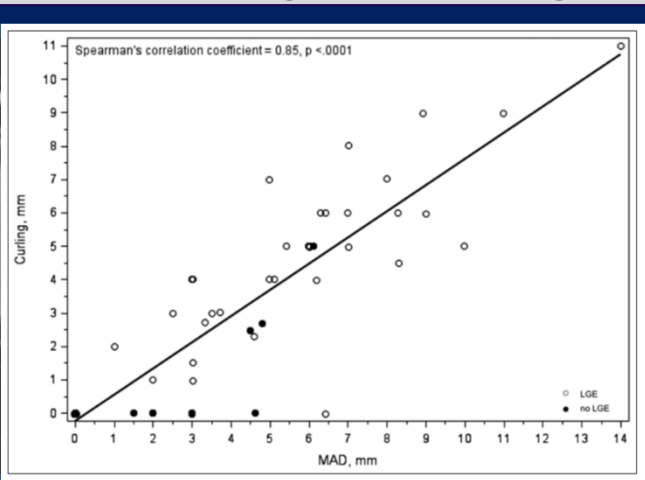
4. MRI findings – 2) Curling





Dejgaard et al, Mitral Annular Disjuncti
JACC 2018, 72:1600-9

Figure 3. Relationship between length of mitral annular disjunction and curling in vivo. A significant correlation (R=0.85) between the depth of curling and length of mitral annulus disjunction (MAD; both expressed as mm) on cardiac magnetic resonance is observed. LGE indicates late gadolinium enhancement.

hofunctional Abnormalities of Mitral Annulus and Mitral Valve Prolapse, Circulation 2016

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4. MRI findings

- 1) MAD ✓
- 2) Curling ✓
- 3) Fibrosis

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4. MRI findings

- 1) MAD ✓
- 2) Curling ✓
- 3) Fibrosis

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4. MRI findings - 3) Fibrosis

Basso, 2015 - Papillary muscle and / or inferobasal wall fibrosis:

- In almost 100% of patients with MVP-related SCD
- Correlated with ventricular arrhythmias origin.
- Structural hallmark of high SCD risk

Basso / Perazzolo et al, Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death, Circulation 2015, 132:556-566

Table 1. Clinical and Pathological Features of 43 Patients Who Died Suddenly With Isolated MVP

Variables	SCD Resulting From MVP (n=43)	Control Subjects (n=15)	*P* Value
MVP leaflet involvement			
Posterior, n (%)	13 (30)	0	…
Bileaflet, n (%)	30 (70)	0	…
Endocardial fibrous plaque, n (%)	25 (58)	0	…
Histology features, n (%)			
LV scar			
PM, n (%)	43 (100)	0	…
Inferobasal wall	38 (88)	0	…
Fibrous tissue /myocardium, % area			
PM, mean±SD	30.5±10.7	6.3±1.6	<0.0001
Inferobasal wall, mean±SD	33.1±7.6	6.4±1.4	<0.0001
Cardiomyocytes diameter, mean±SD, µm	19.2±6.0	12.8±0.4	<0.0001
12-Lead ECG available, n (%)	12 (28)	5 (33)	…
Inverted/biphasic T-wave D2, D3, aVF, n (%)	10 (83)	0	…
VAs, n (%)	12 (28)	0	…
VA morphology, n (%)			
RBBB	12 (100)	0	…
LBBB	8 (67)	0	…

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4. MRI findings - 3) Fibrosis

Letter by Sheppard et al Regarding Article, "Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death"

- Independent cohort of 3680 autopsies → 62 MVP (1.7%)
- LV fibrosis in 74% of cases
  - 1 or both of PMs – predominantly postero-medial PM
  - Adjacent LV wall

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4. MRI findings - 3) Fibrosis

Myocardial Fibrosis in Patients With Primary Mitral Regurgitation With and Without Prolapse

Danai Kitkungvan, MD,[a,b] Faisal Nabi, MD,[a] Raymond J. Kim, MD,[c] Robert O. Bonow, MD, MS,[d] Mohammad A. Khan, MD,[a] Jiaqiong Xu, PhD,[a] Stephen H. Little, MD,[a] Miguel A. Quinones, MD,[a] Gerald M. Lawrie, MD,[a] William A. Zoghbi, MD,[a] Dipan J. Shah, MD[a]

- MVP is associated with more LV fibrosis on MRI compared with non-MVP patients [in primary MR patients]
- Patients with MVP and replacement fibrosis have the highest arrhythmic events (VT, SCD)

TABLE 1 Baseline Characteristics

	MVP (n = 177)	Non-MVP (n = 179)	p Value	Replacement Fibrosis (n = 77)	No Replacement Fibrosis (n = 279)	p Value
CMR findings						
LA volume index, ml/m^2	76.5 ± 31.6	61.8 ± 29.1	<0.001	79.9 ± 31.0	66.1 ± 30.6	<0.001
LVEF, %	66.9 ± 8.4	67.2 ± 8.5	0.79	64.2 ± 7.9	67.8 ± 8.5	<0.001
RVEF, %	53.5 ± 10.3	55.5 ± 8.2	0.04	50.4 ± 11.6	55.6 ± 8.3	<0.001
LVEDV index, ml/m^2	89.4 ± 27.1	71.8 ± 20.5	<0.001	90.6 ± 24.5	77.8 ± 25.2	<0.001
RVEDV index, ml/m^2	75.4 ± 20.8	68.7 ± 23.5	0.005	76.5 ± 22.7	70.8 ± 22.3	0.05
LVESV index, ml/m^2	30.5 ± 14.6	24.4 ± 11.7	<0.001	32.9 ± 13.1	25.9 ± 13.3	<0.001
RVESV index, ml/m^2	36.0 ± 16.2	31.3 ± 14.8	0.005	39.0 ± 18.5	32.1 ± 14.5	<0.001
LV mass index, g/m^2	76.5 ± 24.5	67.6 ± 17.2	<0.001	81.5 ± 22.4	69.4 ± 20.7	<0.001
Mitral RF, %	37.8 ± 15.4	25.0 ± 13.2	<0.001	40.6 ± 14.3	28.8 ± 15.1	<0.001
Mitral RV, ml	45.4 ± 27.3	22.5 ± 15.2	<0.001	47.5 ± 25.4	30.1 ± 23.3	<0.001
MVP	–	–	–	65 (84.4)	112 (40.1)	<0.001
Anterior leaflet	–	–	–	5 (6.5)	16 (5.7)	
Posterior leaflet	–	–	–	39 (50.7)	61 (21.9)	
Bileaflet	–	–	–	21 (27.3)	35 (12.5)	
Flail leaflet	–	–	–	18 (23.4)	22 (7.9)	
Presence of replacement fibrosis	65 (36.7)	12 (6.7)	<0.001	–	–	–

Kitkungvan et al, Myocardial fibrosis in patients with primary mitral regurgitation with and without prolapse, JACC, 2018, Vol 72, 823-34

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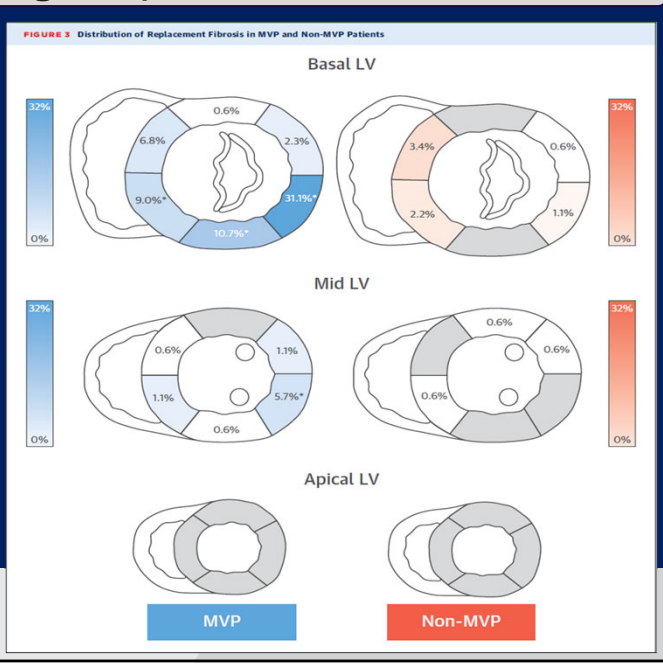
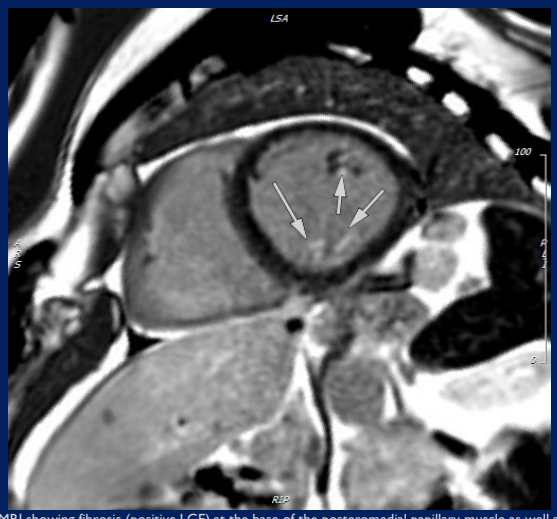
4. MRI findings - 3) Fibrosis

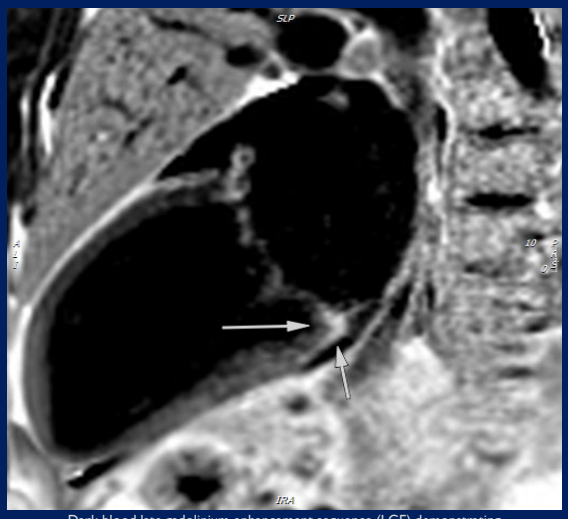
- **Kitkungvan, 2016** - MVP vs non-MVP patients have:
  - More frequent replacement fibrosis in the basal inferolateral wall (31.1%) vs non-MVP patients – basal anteroseptum 3.4%
  - More prevalent replacement fibrosis in the segments adjacent to the posteromedial papillary muscle than non-MVP patients.
- **Bui, 2017**
  - Diffuse nonfocal subclinical fibrosis – associated with complex VAs



4. MRI findings - 3) Fibrosis



MRI showing fibrosis (positive LGE) at the base of the posteromedial papillary muscle as well as minimal fibrosis on the anterolateral papillary muscle



Dark blood late gadolinium enhancement sequence (LGE) demonstrating fibrosis at the level of the posterior mitral annulus

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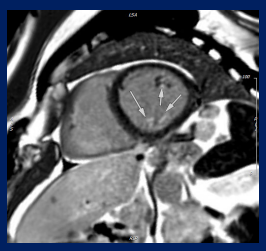
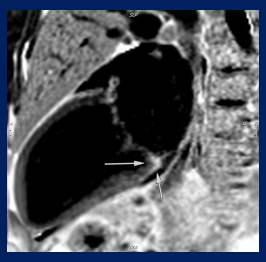
4. MRI findings - 3) Fibrosis





Multifocal PVCs arising from:
- posteromedial papillary muscle
- mitral annulus

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4. MRI findings

- 1) MAD ✓
- 2) Curling ✓
- 3) Fibrosis ✓

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If fibrosis is so important…

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5. Hybrid PET-MRI

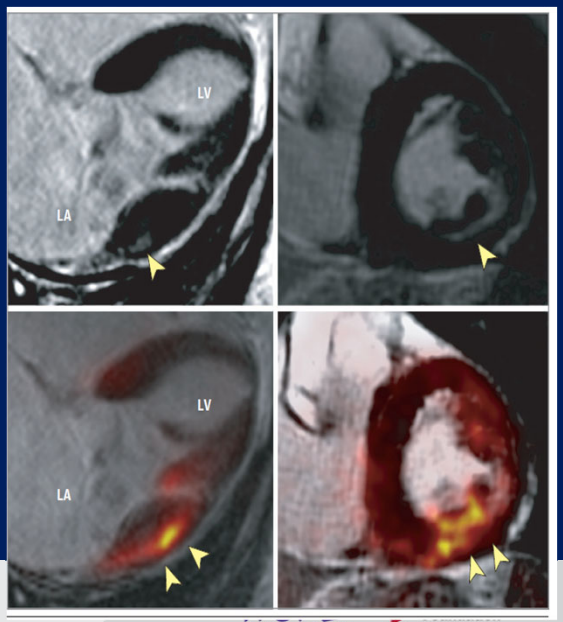
JAMA Cardiology | Original Investigation

Hybrid Positron Emission Tomography/Magnetic Resonance Imaging in Arrhythmic Mitral Valve Prolapse

Marc A. Miller, MD; David H. Adams, MD; Dimosthenis Pandis, MD; Philip M. Robson, PhD; Amit Pawale, MD; Renata Pyzik, MS; Steve L. Liao, MD; Ahmed El-Eshmawi, MD; Percy Boateng, MD; Jalaj Garg, MD; Stephen Waterford, MD; Menachem M. Weiner, MD; Srinivas R. Dukkipati, MD; Vivek Y. Reddy, MD; Zahi A. Fayad, PhD; Maria G. Trivieri, MD, PhD

	FDG +	FDG -
MRI +	14 (70%)	1 (5%)
MRI -	3 (15%)	1 (5%)

- Localization concordance:
  - FDG+: basal-mid infero-lateral and basal-mid anterolateral
  - MRI +: basal mid infero-lateral
- FDG+: minor VAs
- MRI +: complex VAs
- Inflammatory component prodromal to fibrosis?

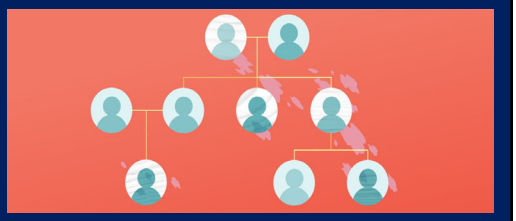


6. Familial clustering

- 6) Family clustering

6. Familial clustering

- Familial clustering described in case reports, pathological series, surgical series
  - Syndromic
  - Nonsyndromic – 3 loci described on chromosomes 11, 16, 13 with mutations in *DCHS1* and *PLP1* genes
- No systematic study of familial SCD in MVP



7. Circulating biomarkers

- 7) Circulating biomarkers

openheart

Increased levels of sST2 in patients with mitral annulus disjunction and ventricular arrhythmias

Esther Scheirlynck,[1,2,3] Lars A Dejgaard,[2,4] Eystein Skjølsvik,[2,4] Oyvind H Lie,[2,4] Andreea Motoc,[3] Einar Hopp,[5,6] Kaoru Tanaka,[3,7] T Ueland,[4,8] Margareth Ribe,[2] Carlos Collet,[3,9] Thor Edvardsen,[2,4] Steven Droogmans,[1,3] Bernard Cosyns,[1,3] Kristina H Haugaa[2,4]

- Soli
  - Higher in patients with MAD and VAs (comp. to patients w/o VA)
  - Proposed as marker of myocardial stretch
- TGFβ1
  - Higher levels in patients with myocardial and papillary muscle fibrosis and larger MAD

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7. "Classic" SCD Risk Factors

Resting electrocardiogram findings
- T-wave inversions in the inferior leads
- QT prolongation
- QT dispersion
- PVCs originating f… RVOT and papillar…
- NSVT and/or VT

Imaging findings

Echocardiogram
Valve-related
…olvement
…kness >5 mm
…ar disjunction
… severe MR
…eaflets
…ctors
…locities of the basal
…l tissue annulus-
… sign
…cal dispersion
…ostsystolic index in basal to …vall
…etected by LGE
…ar disjunction
…ing
… wall hypertrophy

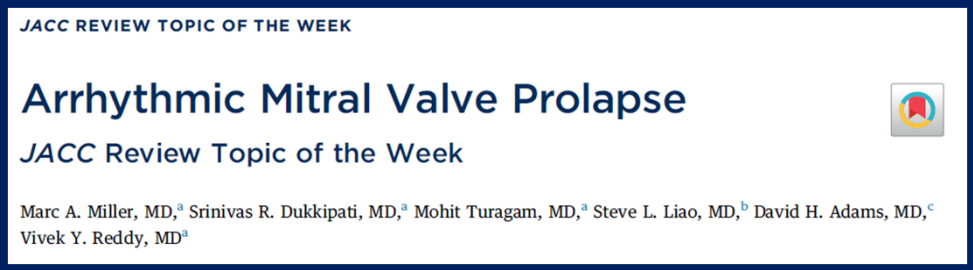
Clinical factors
- Young female
- Palpitations, pres…
- FH of sudden cardiac death
- Exercise-induced polymorphic PVCs, NSVT, VT

Biomarker
- Soluble suppression of tumorigenicity-2

Muthukumar et al, Association Between MVP and SCD, JAMA Cardiology 2020

…nneapolis …art Institute …undation

- 7) EP study



JACC REVIEW TOPIC OF THE WEEK

Arrhythmic Mitral Valve Prolapse

JACC Review Topic of the Week

Marc A. Miller, MD,[a] Srinivas R. Dukkipati, MD,[a] Mohit Turagam, MD,[a] Steve L. Liao, MD,[b] David H. Adams, MD,[c] Vivek Y. Reddy, MD[a]

Risk stratification – EP study

Miller et al, Mt. Sinai:

- If + high risk features and + EPS → Consideration of ICD
- If + high risk features and – EPS → Loop recorder

- Positive EP study:
  - sustained monomorphic VT induced with up to 3 ventricular extrastimuli

    or
  - polymorphic VT or VF induced with up to 2 ventricular extrastimuli

Treatment

- 1) Noninvasive / Medical management
- 2) Catheter based ablation
- 3) ICD
- 4) Mitral valve surgery

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Treatment

- 1) Noninvasive / Medical management
  - Avoid stimulants (caffeine alcohol, tobacco)
  - Beta-blockers
  - Calcium channel blockers
  - Anti-arrhythmic medication…

… improved survival ???

Treatment

- 1) Noninvasive / Medical management
- 2) Catheter based ablation
- 3) ICD
- 4) Mitral valve surgery

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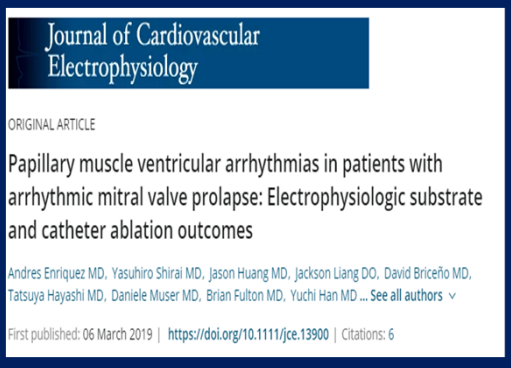
Treatment – 2) Catheter based ablation



Journal of Cardiovascular Electrophysiology

ORIGINAL ARTICLE

Papillary muscle ventricular arrhythmias in patients with arrhythmic mitral valve prolapse: Electrophysiologic substrate and catheter ablation outcomes

Andres Enriquez MD, Yasuhiro Shirai MD, Jason Huang MD, Jackson Liang DO, David Briceño MD, Tatsuya Hayashi MD, Daniele Muser MD, Brian Fulton MD, Yuchi Han MD ... See all authors

First published: 06 March 2019 | https://doi.org/10.1111/jce.13900 | Citations: 6

- 25 patients with MVP
- PVCs mapped to papillary muscles
- 4/9 patients +LGE on MRI

- 76% had complete resolution of PVC with ablation
- 8% had improvement in PVC burden with ablation

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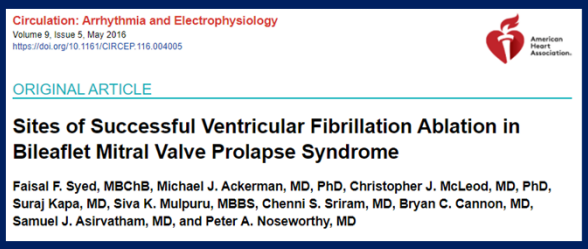
Treatment – 2) Catheter based ablation



- 14 patients with MVP
  - 6/14 w prior SCD (and ICD)
    - all 6 w Purkinje origin VFib (4/6 PM)
  - 8/14 w/o SCD but w symptomatic complex PVCs
    - 5/8 Purkinje origin (3/ PM)

- Acute success of predominant VE foci 17/19 procedures
- Repeat ablation 6/14 patients
- New site of ectopy 2/14 patients
- Symptoms reduced 12/14

➡ *Appropriate ablation of predominant VE foci decreased number of appropriate ICD shocks*

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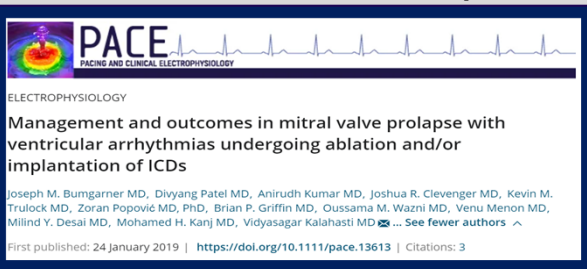
Treatment – 2) Catheter based ablation



- 43/617 patients with MVP and significant VA
- Patients had ICD (30%) or VE ablation (70%)
- Most common foci of VE was left PM
- Successful ablation in 65%
- At 2.6 years mean follow up, 26% had VT recurrence

➡ *While ablation was acutely successful in the majority of cases, there was still a moderate rate of VA recurrence.*

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Treatment

- 1) Noninvasive / Medical management
- 2) Catheter based ablation
- 3) ICD
- 4) Mitral valve surgery

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Treatment

- 1) Noninvasive / Medical management
- 2) Catheter based ablation
- 3) ICD
- 4) Mitral valve surgery

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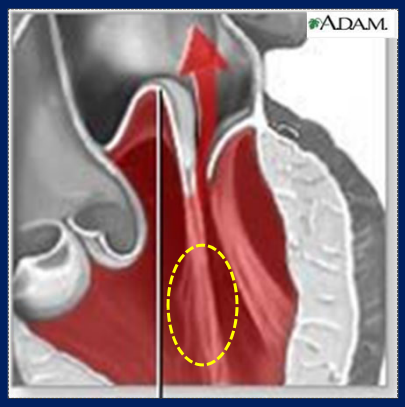
Treatment – 4) Mitral valve surgery

- Relatively limited data…



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Treatment – 4) Mitral valve surgery

Published in final edited form as:
J Interv Card Electrophysiol. 2016 August ; 46(2): 137–143. doi:10.1007/s10840-015-0090-5.

Reduction in Malignant Ventricular Arrhythmia and Appropriate Shocks Following Surgical Correction of Bileaflet Mitral Valve Prolapse

Vaibhav R. Vaidya, MBBS[1], Christopher V. DeSimone, MD, PhD[2], Namrata Damle, BS[3], Niyada Naksuk, MD[2], Faisal F. Syed, MBChB[4], Michael J. Ackerman, MD, PhD[2,5,6], Shiva P. Ponamgi, MD[7], Vuyisile T. Nkomo, MD, MPH[2], Rakesh M. Suri, MD, DPhil[8], Peter A. Noseworthy, MD[2], and Samuel J. Asirvatham, MD[2,5]

- 8 pts with BiMVP and ICD both pre- and post-MVR
- MVR reduced the number of appropriate ICD shocks

	Preoperative				Postoperative				Mortality
	VT	VF	Appropriate shock	Inappropriate shock	VT	VF	Appropriate shock	Inappropriate shock	
1	0	5	3	0	0	0	0	0	Alive
2	1	2	4	0	2	0	2	1	Alive
3	0	1	1	0	0	0	0	0	Alive
4	4 (VT/VF)		4	1	0	0	0	0	Alive
5	7	0	7	0	0	1	2	1	Alive

Treatment – 4) Mitral valve surgery

Contents lists available at ScienceDirect

Indian Pacing and Electrophysiology Journal

journal homepage: www.elsevier.com/locate/IPEJ

The effect of mitral valve surgery on ventricular arrhythmia in patients with bileaflet mitral valve prolapse

Niyada Naksuk [a], Faisal F. Syed [b], Chayakrit Krittanawong [a], Mark J. Anderson [c], Elisa Ebrille [d], Christopher V. DeSimone [a], Vaibhav R. Vaidya [a], Shiva P. Ponamgi [e], Rakesh M. Suri [f], Michael J. Ackerman [a, g, h], Vuyisile T. Nkomo [a], Samuel J. Asirvatham [a, g], Peter A. Noseworthy [a, *]

Treatment – 4) Mitral valve surgery

- 32 patient with MVP undergoing MV surgery for MR sec to BiMVP
- Pre- & post-op Holter
  - ≥10% VA burden decrease
  - <10% VA burden decrease
- Patients w significant decrease in VA burden were younger (~42 yo, <60 yo)

Clinical characteristics of study patients with and without a significant reduction in ventricular ectopy after mitral valve surgery.

	All patients (N = 32)	Group A (N = 17)	Group B (N = 15)	*P* value
Age, years, (mean ± SD)	63.5 ± 12.8	59.3 ± 15.2	68.2 ± 7.2	0.04
Female, No. (%)	17 (53.1)	7 (41.2)	10 (66.7)	0.15
Pre-operative NYHA class III/IV, No. (%)	9 (28.1)	5 (29.4)	4 (26.7)	1.00
Pre-operative reported palpitations, No. (%)	19 (59.4)	9 (52.9)	10 (66.7)	0.43
Pre-operative antiarrhythmic drugs[a], No. (%)	18 (56.3)	10 (58.8)	8 (53.3)	0.75
Post-operative antiarrhythmic drugs[b], No. (%)	21 (65.6)	11 (64.7)	10 (66.7)	0.91
Pre-operative atrial fibrillation, No. (%)	14 (43.8)	6 (35.3)	8 (53.3)	0.30
Pre-operative T-wave abnormalities, No. (%)	10 (31.4)	6 (35.3)	4 (26.7)	0.39
Mitral Valve appearance				
Flail, No. (%)	8 (25.0)	4 (23.5)	4 (26.7)	1.00
Myxomatous, No. (%)	13 (40.6)	9 (52.9)	4 (26.7)	0.17
Surgery				
Mitral valve repair, No. (%)	30 (93.8)	16 (94.1)	14 (93.3)	1.00
Papillary muscle manipulation, No. (%)	11 (34.38)	5 (29.4)	6 (40.0)	0.53
CABG, No. (%)	6 (18.8)	3 (17.7)	3 (20.0)	0.86
Preoperative Holter				
Time of Holter monitors to time of surgery, days, median [IQR]	98 [39, 557]	98 [27, 394]	126 [43, 712]	0.41
Preoperative VE frequency, bph, median [IQR]	41 [16, 196]	102 [31, 430]	30 [5, 130]	0.05
Postoperative Holter				
Time of surgery to time of Holter monitors, days, median [IQR]	102 [47, 213]	68 [33, 215]	170 [85, 217]	0.67
Postoperative VE frequency, bph, median [IQR]	40 [5, 186]	34 [3, 197]	183 [8, 270]	0.12
Percent change, %, median [IQR]	−13 [-77, 54]	−76 [-91, −40]	57 [42, 538]	0.03
Absolute changes in VE frequency, bph, median [IQR]	−3 [-104, 23]	−99 [-290, −12]	28 [5, 158]	0.01

- There are some easily identifiable high risk SCD features in patients with MVP
  - Bileaflet MVP
  - Purkinje-origin Vas
  - Severe VAs
  - Pickelhaube sign
  - MAD
  - Speckle tracking (supra-normal contraction, incoordinate contraction)
  - Specific areas of replacement fibrosis

- Designing a cost-effective risk stratification model to identify patients at risk still remains a challenge
- Optimum treatment (medical, interventional, ICD, surgical correction) and optimal timing of intervention still remains unclear
- Awareness of this condition and individualized patient treatment remains paramount

HOPE DISCOVERED HERE

Minneapolis Heart Institute Foundation

Thank you!

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