The Arrhythmic Mitral Valve Prolapse

MHIF-2023

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Minneapolis Heart Institute

DMR and MVP

Sudden death
72 yo asymptomatic man with DMR

- R = 0.84
- TVI = 270 cm
- Vmax = 690
- ERO = 0.30 cm²
- RVol = 84 cc/beat

72 years old gentleman with MR
MR quantitation

- TVI = 270 cm
- Vmax = 690
- ERO = 0.30 cm²
- RVol = 84 cc/beat
Peak exercise VT

Patient still not interested in surgery

Ex testing:
- 12 mins on O2 protocol
- Double product: 31,000
- Peak VO2:
  - 26 ml/kg/min or 107% of expected

1 month after last visit: Cardiac arrest

- 'He was sitting on packing box, then slumped over and was found on the floor unresponsive.'
  - 911 was called, Patient found in VFib.
  - Patient was shocked twice. Returned to sinus rhythm

In Hospital
- EKG: sinus rhythm, 86/mn

Physical examination: O2sat 97% on room air, BP147/84, no sign of pulmonary edema, systolic murmur 3/6

CT: No evidence of hemorrhage, with a small lacunar infarct in the right subinsular region
- Coronary and LV angiograms
CORONARY Summary
- middle LAD is 40% obstructed by a single discrete lesion
- First marginal branch is 60% obstructed by a single lesion
- middle RCA by a single mild discrete lesion

LV Gram
- Mild LV dilatation, EF 59%
- Moderate MR ?

CARDIAC SURGERY
- Mitral valve repair
- Coronary artery bypass grafting IMA to LAD, SVG OM
- Then ICD implantation……no further discharge!
Sudden Death in Mitral Regurgitation Due to Flail Leaflet

25/348 Patients, Age 71 ± 9 Yrs

- Male 84%
- Atrial fibrillation (36%)
- Hypertension (28%)
- Posterior leaflet (87%)

MR Due to Flail Leaflet Mode of Death

- Total mortality
- Cardiac mortality
- Sudden death

Incidence (%)

Years after diagnosis

53 ± 5
43 ± 5
19 ± 4
Mitral Regurgitation
Sudden Death Rate

1.8% per year

Yearly Rate of Sudden Death

%/year

NYHA

I

II

III-IV

Sudden Death in MR
Due to Flail Leaflet

Sudden Death Events/Group

NYHA

I

II

III-IV

7.8±3.2

10

9

6
Sudden Death in MR
Due to Flail Leaflet

Yearly Rate of Sudden Death

Sudden Death Events/Group

LVEF (%)
≥60 50-59 <50

1.5±0.4 0.9±0.6 12.7±5.2

≥60 50-59 <50

17 2 6

Sinus rhythm
Atrial fibrillation

JACC 34:2078, Dec 1999
Mitral Regurgitation

Sudden Death Rate

No Risk Factor
0.8% per year

Effect of Surgery
Hazard Ratio
0.29 [0.11-0.72]

Degenerative MR

Sudden Death

• Notable proportion of overall mortality of DMR
• More frequent with Sx, low EF, AF
• SD events may occur without risk factors
• SD rate is markedly reduced by Mitral Surgery
Operating on patients with no or minimal symptoms restores life expectancy.

Organic MR main determinant of outcome: Mitral Valve Repair

- Aortic mitral fibrosa
- Anterior lateral commissure
- Aortic leaflet
- Posterior medial commissure
- Anterior leaflet
- Posterior leaflet
- Normal
- Flail posterior leaflet
- Resection of flail segment
- Repaired mitral valve
Association Between Early Surgical Intervention vs Watchful Waiting and Outcomes for Mitral Regurgitation Due to Flail Mitral Valve Leaflets

Rakshah M. Sarl, MD, CPHE, Jean-Louis Venovaschakla, MD, Francesco Sgadrito, MD, PhD, Herzl V. Schiff, MD, Christopher Treadway, MD, Jean-Francois Akavos, MD, Andrea Elbarbary, MD, Agnete Pircquet, MD, Marlonia Vaz-Neto, PhD, Dan Ruderer, MD, Antonio Russo, MD, Pietro I. Micali, MD, Marko Truong, MD

**IMPORTANCE** The optimal management of severe mitral valve regurgitation in patients without class I triggers (heart failure symptoms or left ventricular dysfunction) remains controversial in part due to the poorly defined long-term consequences of current management strategies. In the absence of clinical trial data, analysis of large multicenter registries is critical.

**OBJECTIVE** To ascertain the comparative effectiveness of initial medical management (non-surgical observation) vs early mitral valve surgery following the diagnosis of mitral regurgitation due to flail leaflets.

**DESIGN, SETTING, AND PARTICIPANTS** The Mitral Regurgitation International Database (MRI) registry includes 2097 consecutive patients with flail mitral valve regurgitation (MR) who underwent surgery (465) vs medical management (1632). Mean follow-up was 10.3 years and was 96% complete. Of ICU patients with mitral regurgitation without the American College of Cardiology (ACC) and the American Heart Association (AHA) guideline class I triggers, 57% patients were initially medically managed and

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**Figure 1. Survival After Diagnosis of Mitral Regurgitation Due to Flail Mitral Leaflet According to Initial Treatment Strategy**

- **A.** Overall population
  - Early surgery
  - Medical management

- **B.** Frequency score-matched cohort
  - Early surgery
  - Medical management
Degenerative MR

Sudden Death

In patients with DMR moderate or severe, the best prevention of SD is:
Elective mitral valve repair
Performed at low-risk
With requirement of “Perfection”
Mitral Valve Prolapse
Outcome is a great source of Confusion

Few Complications

We are confused by discordant data on MVP outcome
Cardiologists used to call that Mitral Valve Prolapse?

The Saddle-shape of the Mitral annulus

Three-Dimensional Echocardiographic Reconstruction of the Mitral Valve, With Implications for the Diagnosis of Mitral Valve Prolapse

Robert A. Levine, MD, Mark D. Handschumacher, BS, Anthony J. Santillippo, MD, Albert A. Lagezi, MD, Pamela Harrigan, RDMS,
Mitral Valve Prolapse

Prevalence of MVP

Previously overestimated 5-17%

With current criteria 0.6-2.4%
Sudden Death in the Mitral Valve Prolapse-Click Syndrome

ROBERT M. JERESATY
Hartford, Connecticut

The mitral valve prolapse click syndrome continues to cause much concern and debate. The electrocardiogram (ECG) shows a pattern consistent with refractory ventricular tachycardia and fibrillation in a patient with the prolapsing mitral leaflet syndrome: successful control with overdrive pacing.

RHYTHM STRIPS (MCL I)

5:00 PM

5:30 PM

6:00 PM

The New England Journal of Medicine

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ECHOCARDIOGRAPHICALLY DOCUMENTED MITRAL-VALVE PROLAPSE

Long-Term Follow-up of 237 Patients

Table 2: Association of Complications with Redundancy of Mitral-Valve Leaflets in 237 Patients with Mitral-Valve Prolapse.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Redundant (n = 97)</th>
<th>Nonredundant (n = 140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Cerebral embolic event*</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total (%)</td>
<td>10 (10.3)</td>
<td>1 (0.7)</td>
</tr>
</tbody>
</table>

*in patients in normal sinus rhythm.
Mitral Valve Prolapse

Prevalence and Clinical Outcome of Mitral Valve Prolapse

The New England Journal of Medicine July 1st, 1999

<table>
<thead>
<tr>
<th>Clinical Finding</th>
<th>Mitral-Valve Prolapse (N=84)</th>
<th>No Mitral-Valve Prolapse (N=3407)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. (%)</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0 (0.7)</td>
<td>25 (0.7)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1 (1.2)</td>
<td>58 (1.7)</td>
</tr>
<tr>
<td>Cerebrovascular disease*</td>
<td>1 (1.2)</td>
<td>52 (1.5)</td>
</tr>
<tr>
<td>Syncope</td>
<td>3 (3.6)</td>
<td>103 (3.0)</td>
</tr>
</tbody>
</table>

*Cerebrovascular disease refers to stroke or transient ischemic attack.

Mitra Valve Problems Are Not So Serious After All

As many as 28 million Americans who were told they are in danger of stroke, heart failure and other problems because of mitral valve prolapse probably don’t have to worry. A new study showed that about 6.4 percent of the population—not the 10 percent prior studies had estimated—have the condition.

Is MVP Really and Uniformly Benign?

Independent of age and sex, the risk of sudden death and stroke was found to be higher in MVP patients than in the general population. However, the risk of death from cardiac reasons was lower in MVP patients.

Natural History of Asymptomatic Mitral Valve Prolapse in the Community

Jean-François Avierinos, MD; Bernard J. Gersh, MB, ChB, DPhil; L. Joseph Melton III, MD; Kent R. Bailey, PhD; Clarence Shub, MD; Rick A. Nishimura, MD; A. Janill Tajik, MD; Maurice Enriquez-Sarano, MD

Background—The outcome of mitral valve prolapse (MVP) is controversial, with marked discrepancies in reported complication rates.

Methods and Results—We conducted a community study of all Olmsted County, Minn, residents first diagnosed with asymptomatic MVP between 1989 and 1998 (N=833). Diagnosis, motivated by auscultatory findings (n=557) or incidental (n=276), was always confirmed by echocardiography with the use of current criteria. Endpoints analyzed were cardiovascular mortality (n=117), MVP-related events (n=109), and noncardiovascular mortality (n=276). The most frequent primary risk factors for cardiovascular mortality were mitral regurgitation from moderate to severe (P=0.002, n=131) and, less frequently, ejection fraction <50% (P=0.003, n=31). Secondary risk factors independently predictive of cardiovascular mortality were slight mitral regurgitation, left atrium ≥40 mm, atrial fibrillation, and age ≥50 years (all P<0.01). Patients with only 0 or 1 secondary risk factor (n=430) had excellent outcome, with 10-year mortality of 5.2% (P=0.001 versus expected), cardiovascular mortality of 0.5%/y, and MVP-related events of 0.2%/y. The second secondary risk factor (n=250) had mortality similar to expected (P=0.20) but high cardiovascular mortality (6.2%/y, P<0.01) and notable MVP-related events (1.7%/y, P<0.01). Patients with primary risk factors (n=153) showed excess 10-year mortality (45.2%/y, P=0.01 versus expected), high mortality (18.5%/y, P<0.01), and high MVP-related events (15%/y, P<0.01).

Conclusions—Natural history of asymptomatic MVP in the community is widely heterogeneous and may be severe. Clinical and echocardiographic characteristics allow separation of the majority of patients with excellent prognosis from subsets of patients displaying, during follow-up, high morbidity or even excess mortality as direct a consequence of MVP. (Circulation. 2002;106:1355-1361.)
Asymptomatic MVP in the Population

Mortality and Morbidity

Years after diagnosis

Events (%)

CV morbidity
Overall mortality
CV mortality

Asymptomatic MVP in the Population

Primary Risk Factors (mort)
• EF<50%
• MR ≥ moderate

Secondary Risk Factors (morb)
• Age ≥ 50 years
• A Fib
• Slight MR
• Flail leaflet
• LA ≥ 40 mm
**Outcome of MVP – Risk Stratification**

3 groups

<table>
<thead>
<tr>
<th>RF Category</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No or 1 secondary RF</td>
<td>430</td>
<td>52</td>
</tr>
<tr>
<td>≥2 secondary RF</td>
<td>250</td>
<td>30</td>
</tr>
<tr>
<td>Primary RF</td>
<td>153</td>
<td>18</td>
</tr>
</tbody>
</table>
  - MR ≥ moderate                | 131 |
  - EF <50%                      | 31  |

**Natural History of Asymptomatic Mitral Valve Prolapse in the Community**

Jean-François Avronnais, MD; Bernard J. Garsh, MB, ChB, DPhil; L. Joseph Melina III, MD; Kent R. Bailey, PhD; Clarence Shih, MD; Nick A. Nolensia, MD; A. Jemal Tank, MD; Maurice Enriquez-Sarano, MD

- **Overall Survival**
  - No or 1 secondary RF: 95 ± 2%
  - ≥2 secondary RF: 70 ± 5%
  - Primary RF: 55 ± 9%
  - Overall survival: P<0.001

- **Cardiac Survival**
  - No or 1 secondary RF: 87 ± 4%
  - ≥2 secondary RF: 87 ± 4%
  - Primary RF: 66 ± 10%
  - Cardiac survival: P<0.001
All studies confirm:

- **MR severity** is the major determinant of MVP outcome
- **Poor outcome** in the group with severe MR
- **Benign outcome** in the group with no/mild MR
Mitral Valve Prolapse and Sudden Death

“…Our son, Crick, had mitral valve prolapse. I think he is the only one who died suddenly of thousands of patients I’ve seen with mitral valve prolapse.”

W. Proctor Harvey, MD, FACC: Conversations with the Editor
William C. Roberts, MD

Am J Cardiol 89:435, Feb 15, 2002

Table 1: Demographics of OHCA Cohort (n=258)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>No MVP</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at sentinel event (yrs)</td>
<td>14/24</td>
<td>0.94</td>
</tr>
<tr>
<td>Women</td>
<td>99/101</td>
<td>0.04</td>
</tr>
<tr>
<td>QTc Interval (msec)</td>
<td>428 = 28</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiac arrest at hospital</td>
<td>8/10(80%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Activity at time of arrest</td>
<td>5/6 (83%)</td>
<td>0.04</td>
</tr>
<tr>
<td>8 waking rest, 7 acute</td>
<td>9 waking rest, 5 acute</td>
<td>0.60</td>
</tr>
<tr>
<td>8 waking rest, 2 acute</td>
<td>emotional or physical</td>
<td></td>
</tr>
<tr>
<td>8 waking rest, 2 acute</td>
<td>emotional or physical</td>
<td></td>
</tr>
<tr>
<td>8 waking rest, 7 acute</td>
<td>emotional or physical</td>
<td></td>
</tr>
<tr>
<td>8 waking rest, 5 acute</td>
<td>stress, 0 sleep</td>
<td></td>
</tr>
<tr>
<td>ICD implantation</td>
<td>14/1 (100%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Followup after ICD placement</td>
<td>8/24 (80%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Did they die with MVP?
Or
Did they die because of MVP?
How do we recognize one in a crowd?

650 SCD age<40

MVP =43, 6.6%

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

<table>
<thead>
<tr>
<th>Variables</th>
<th>SCD Resulting From MVP (n=42)</th>
<th>Control Subjects (n=15)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVP leaflet involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior, n (%)</td>
<td>13 (30)</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>Bileaflet, n (%)</td>
<td>30 (70)</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>Endocardial fibrous plaque, n (%)</td>
<td>25 (58)</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>Histology features, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV scar</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM, n (%)</td>
<td>43 (100)</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>Interventricular wall</td>
<td>38 (88)</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>Fibrous tissue/myocardium, % area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM, mean±SD</td>
<td>30.5±10.7</td>
<td>6.3±1.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Interventricular wall, mean±SD</td>
<td>33.1±7.6</td>
<td>6.4±1.4</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Isolated MVP and SUD

There a typical phenotype found in SD associated with isolated MVP:

- Clinically: Syncope/presyncope
- Echo: severe myxomatous disease with annular disjunction
- ECG: PVC-VT from PPM or annulus
26 y.o. with hx of presyncope
works as nursing aid
SCA due to VF requiring 8
defibrillation for SR return

MAD, the red alert?

To prevent the exponential increase in costs, referrals,
and false-positive results, only MVP patients with
red flags, particularly MAD and systolic curling, besides
arrhythmic presentation, will undergo further investigation,
including contrast-enhanced or T1 mapping CMR
and a strict arrhythmia surveillance for proper management
and SCD prevention.
What is the Mitral Annulus?

Normal atrio-valve and ventricle junction
Thin leaflets

Hutchins GM, NEJM 1986; 314: 535-40
What is the Mitral Annulus Function?

Left Atrial Function
What is the Mitral Annulus Function?

- AP contraction
- Saddle-shape accentuation
- AP contraction
Mitral Annulus Disjunction

Hutchins GM, NEJM 1986; 314: 535–40

Mitral Annulus Disjunction

Mitral Annulus Disjunction
Surgical inspection

Eriksson MJ, JASE 2005; 18; 1014-22
MAD DIAGNOSIS

TTE of MAD definition dynamic evaluation step-by-step approach with careful visualisation of MV annulus in PSLA view

MAD = DETACHMENT OF THE INSERTION FROM THE LV MYOCARDIUM

MADFRAME BY FRAME

INSERTION OF THE POSTERIOR LEAFLET

MADFRAME BY FRAME

FRAME BY FRAME

INSULATION OF THE POSTERIOR LEAFLET

MADFRAME BY FRAME
MAD diagnosis

MAD diagnosis requires:
- Recognition of the mitral annulus position frame by frame in LAX views throughout systole, then
- Detection of separation annulus-LV myocardium at mid and late-systole
- Determination of MVP depth from the annulus position
MAD diagnosis requires:
- Recognition of the mitral annulus position frame by frame in LAX views throughout systole, then
- Detection of separation annulus-LV myocardium at mid and late-systole
- Determination of MVP depth from the annulus position

Imaging must provide sufficient spatial and temporal resolution to quantify MAD and MVP
Context & Physiologic Consequences of MAD?
More myxomatous leaflets, larger and systolic-expanding annulus
31% 69%
30% 70%
81%
Mitral Valve Prolapse

is MAD.........the Angel of Death?

Presentation and Outcome of Arrhythmic Mitral Valve Prolapse

AMVP PHENOTYPE
**Phenotypic risk features:**
TWI in the inferior leads, multiple polymorphic PVCs, MAD, redundant MV leaflets, enlarged LA, LV-EF ≤ 50%, LGE.
Arrhythmic MVP is independently associated with MAD but excess-mortality is observed only with severe arrhythmias (NSVT>180) and very progressively over time.
The Mitral Annular Disjunction of Mitral Valve Prolapse
Presentation and Outcome

Benjamin Essayagh, MD, Avi Sabbag, MD, Clémence Antoine, MD, Giovanni Benfari, MD, Roberta Batista, MD, Li-Tan Yang, MD, Joseph Maalouf, MD, Prabin Thapa, MSc, Samuel Asirvatham, MD, Hector I. Michanela, MD, Maurice Enriquez-Sarano, MD
Mitral Annular Disjunction is:
A manifestation of severely
myxomatous MVP,
An independent determinant of
AMVP, but
Survival is maintained within the
first 10-year FU

Mitral Valve Prolapse
MAD is not the Angel of Death
but advocates fc AMVP monitoring
Sudden death-DMR MVP
SD is an important issue in myxomatous diseases

DMR: Notable SD rate. Approach to prevent SD is early repair

Isolated MVP: SD is infrequent but risk is recognized by the triad Syncope/MAD/High-risk VT
AMVP is a real entity

Detect the phenotype with highest propensity for development of Ventricular Arrhythmias

Detect the Arrhythmias by monitoring, if necessary prolonged, if necessary repeated

Treat Arrhythmias based on their severity and association to DMR

THANK YOU