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# One not to miss…The Arrhythmic Mitral Valve Prolapse Syndrome

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## Take Home Messages

- Mitral valve prolapse is the most common valvular heart disease and historically was considered benign in the absence of severe mitral regurgitation and preserved left ventricular function.
- A new emerging subset associated with sudden cardiac death that does not follow traditional risk stratification has been established, termed the arrhythmic mitral valve prolapse (A-MVP) syndrome.
- A-MVP poses a clinical challenge in identifying those at risk of lethal arrythmias that may benefit from a primary prevention implantable cardiac defibrillator. Ultimately further research is required to improve risk stratification.

**Introduction:**

Mitral valve prolapse (MVP) is the most common valvular heart disease in developed countries, with a prevalence of 2-3% across the general population (1). It is associated with connective tissue diseases and a genetic component has been described; the presence of parental MVP has been found to increase risk 5-fold (2). It is clinically defined as a systolic superior displacement of one or both mitral valve leaflets, >2mm above the plane of the mitral annulus. MVP is heterogenous but two distinct phenotypic subsets are defined: (i) myxomatous (Barlow's) disease, characterised by excess tissue and chordal thickening/elongation, as a result of a non-inflammatory, progressive disarray of valve structure and (ii) fibroblastic deficiency, characterised by chordal thinning and a higher probability of chordae rupture (1).

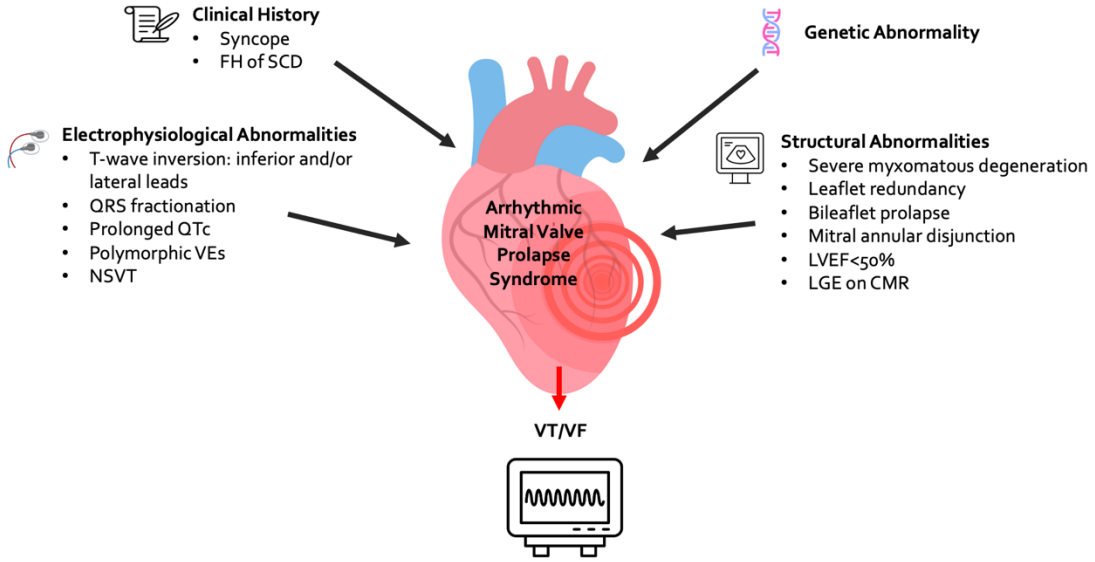
There is a small appreciated <1% risk of sudden cardiac death (SCD) in MVP (1). Traditional risk factors include severe associated mitral regurgitation (MR) and left ventricular (LV) systolic

dysfunction. If absent, the condition was classically felt benign (3,4,5). However, an emerging malignant subset termed the "arrhythmic mitral valve prolapse (A-MVP) syndrome" has been identified. This group associate with a greater risk of complex arrythmia and SCD in the presence of a normal LV function and non-severe MR, creating a risk stratification challenge. The syndrome is clinically defined as the presence of MVP with evidence of frequent (>5% burden of ventricular ectopy) or complex ventricular arrythmias (VAs) (non-sustained ventricular tachycardia (VT), VT, ventricular fibrillation (VF)), in the absence of an alternative well-defined arrhythmic substrate (1).

*Phenotypic description of A-MVP:*

A phenotypic picture of A-MVP has emerged that distinguishes the syndrome from general MVP (figure 1) (1,6,7,8,9). A family history of SCD and syncope are established associations (1). Structural abnormalities include high degree myxomatous degeneration of valve leaflets, leaflet redundancy, bi-leaflet prolapse and the presence of mitral annular disjunction, defined as a systolic separation between the mitral annulus supporting the posterior mitral leaflet and the ventricular myocardium (10,11,12). Late-gadolinium enhancement (LGE) suggestive of myocardial fibrosis and scar (identified on Cardiac Magnetic Resonance (CMR) imaging) located specifically around the mitral valve apparatus and adjacent LV wall has also been associated (13,14). Electrophysiological markers include ECG abnormalities such as T-wave inversion in inferior and lateral leads, QTc prolongation and fragmented QRS complexes. Complex/frequent ventricular arrythmias, including polymorphic ventricular ectopy (PVE) from papillary muscles and fascicular regions and non-sustained VT are also linked (1). These phenotypic features link to the current hypothesis of arrhythmogenesis in A-MVP, where mechanical traction from the prolapsing valve is thought to induce regionalised reactive fibrotic, cellular and molecular changes, promoting micro re-entry and enhanced automaticity. This culminates in pro-arrhythmic alternations of the action potential, reflecting observations such as T-wave inversion and QTc lengthening (1).

**Figure 1:** Summary of the observed phenotype in arrhythmic mitral valve prolapse syndrome.




*Arrhythmic risk stratification in MVP:*

A combination of the phenotypic features that characterise A-MVP can together paint a high-risk picture of lethal arrythmia. However, a challenge occurs when they exist in isolation or low numbers. For example, isolated T-wave inversion is observed in around 40% of MVP without a history of sustained VAs, PVEs are common and SCD has been reported without fibrosis on CMR (1,9,15). These heterogeneities in MVP highlight the challenge when attempting to predict SCD risk. There is also added uncertainty due to a relative lack of long-term follow-up studies and clinical trials in the cohort, highlighted as an evidence gap in international consensus guidance. This guidance reflects the state uncertainty, advising an ICD as "reasonable" for primary prevention when only certain risk factors are present (1). It also attests to the need of further research on the impact of anti-arrhythmic therapies, PVE/VT ablation, and MV replacement/repair on prognosis in A-MVP.

## Conclusion:

A-MVP syndrome is an emerging subgroup associated with SCD that does not follow traditional risk stratification. The cohort poses a clinical challenge in identifying those at risk of lethal arrythmias that may benefit from a primary prevention ICD. Further study is required and

management is currently best delivered via a multidisciplinary team approach referring to international consensus guidance (1).

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