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Mitral valve prolapse and sudden cardiac death: A perspective on risk-stratification

"[Mitral valve prolapse] is a completely benign and trivial condition...In my mind it rates in importance with freckles...occurrence of sudden death among young healthy women is so rare as to be almost unheard of."

—Bernard Lown, MD¹

A 45-YEAR-OLD WOMAN with a history of mitral valve prolapse is admitted to the hospital after a cardiac arrest. She was found unresponsive at a local library, received early bystander cardiopulmonary resuscitation, and was found to be in ventricular fibrillation by emergency medical services. Return of spontaneous circulation was achieved, and she was taken to the hospital for further workup and evaluation.

Her electrocardiogram on admission showed normal PR, QRS, and QT intervals and biphasic T waves in leads II, III, and aVF. Coronary angiography revealed normal coronary anatomy. Echocardiography showed bileaflet mitral valve prolapse with mild to moderate mitral regurgitation. Frequent premature ventricular contractions were noted on telemetry throughout her hospitalization. She underwent placement of an implantable cardioverter-defibrillator (ICD) without complications and was discharged home after an 8-day hospitalization.

This case illustrates a patient who had a rare but significant complication of mitral valve prolapse: sudden cardiac death. Although mitral valve prolapse (previously known as Barlow disease) has been associated with sudden cardiac death for decades,² a causal relationship has been difficult to ascer-

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tain, given the significant prevalence of mitral valve prolapse in the general population (about 2%, more common in women) and the challenge of determining a specific etiology of sudden cardiac death postmortem.^{3,4}

■ A 'MALIGNANT' PHENOTYPE OF MITRAL VALVE PROLAPSE

Over time, observational data have accumulated regarding patients with mitral valve prolapse who survived a fatal ventricular arrhythmia in whom no other cause could be found, such as long or short QT syndrome, Brugada syndrome, or coronary or other arrhythmogenic structural heart disease. Together, these studies have demonstrated a "malignant" phenotype of mitral valve prolapse, with specific associated structural, extravalvular, and arrhythmogenic features.⁵ These higher-risk characteristics include:

- Female sex
- Biphasic or inverted T waves in at least 1 inferior lead (II, III, aVF)
- Frequent premature ventricular contractions
- Bileaflet prolapse
- Evidence of papillary muscle fibrosis on cardiac magnetic resonance imaging.³⁻⁷

The mechanisms by which these characteristics increase the risk of sudden cardiac death are still not completely understood, but they are likely multifactorial and involve abnormal function or strain of the mitral valve apparatus, abnormalities in the conduction system, and cardiac responsiveness to nervous system and hormonal input.⁵

Mitral valve prolapse is common, but sudden cardiac death is rare; how can we stratify risk?

■ OUR EXPERIENCE

Even though sudden cardiac death in mitral valve prolapse is rare, our hospital system has some (albeit limited) experience with it. In recent years we have had 6 patients who had an episode of sudden cardiac death or ventricular tachycardia in the setting of mitral valve prolapse without another explanation for their fatal arrhythmia. Of these 6 patients:

- 5 were female
- 5 had inverted or biphasic T waves in at least 1 inferior lead
- 5 had premature ventricular contractions
- 3 had bileaflet prolapse
- 1 had papillary muscle fibrosis on cardiac magnetic resonance imaging (only 5 of the 6 underwent magnetic resonance imaging).

All of these high-risk patients were identified after developing a fatal ventricular arrhythmia or cardiac arrest, and all of them had an ICD placed for secondary prevention. Although this is a limited case series, it is congruent with what has been found in larger observational data sets and systematic reviews.⁴

■ OUR PERSPECTIVE

Based on the limited data available and on our clinical experience, we generally recommend further risk-stratification with exercise stress testing in patients who present with a diagnosis of mitral valve prolapse and other high-risk features, such as bileaflet prolapse and high-risk electrocardiographic findings. Exercise-related premature ventricular contractions or nonsustained ventricular tachycardia, especially with shorter coupling intervals, puts these patients at higher risk of developing a fatal ventricular arrhythmia.

Further risk-stratification may be considered in the form of electrophysiologic testing, during which induction of sustained ventricular tachycardia can be attempted in a controlled setting. This strategy helps determine which patients with mitral valve prolapse are most likely to benefit from ICD placement for primary prevention of sudden cardiac death, and thus may be lifesaving. The role of electrophysiologic testing, however, is undergoing further evaluation.

■ STUDY IS NEEDED

This proposed approach has several important limitations, however. The Heart Rhythm Society does not provide decisive guidelines for appropriate risk-stratification in patients with mitral valve prolapse, and there are no recommendations on prophylactic ICD placement for primary prevention in patients with mitral valve prolapse and high-risk characteristics. Given the lack of prospective data or randomized controlled trials in this area, the associated high-risk characteristics are based on retrospective analyses and reviews, which are prone to selection bias and publication bias.

Key questions remain:

- Which patients should be screened routinely for the high-risk mitral valve prolapse phenotype?
- Which methods of screening would be most cost-effective?
- What are the positive and negative predictive values of inducible ventricular tachycardia for sudden cardiac death? (No randomized prospective study has yet addressed this topic.)
- Does repairing or replacing the mitral valve decrease the risk of sudden cardiac death in patients with the high-risk phenotype?

Currently, a nonrandomized clinical trial is recruiting patients to undergo cardiac magnetic resonance imaging, exercise stress testing, and ambulatory external loop recording to assess if the level of mitral valve regurgitation increases the risk of ventricular arrhythmia.⁸ Hopefully, the findings of this study will help practicing clinicians make more informed decisions as to which patients require further risk-stratification and possible intervention to reduce the risk of ventricular arrhythmias.

Mitral valve prolapse is common and, in general, should not cause significant alarm to patients or clinicians. However, we would argue that patients with mitral valve prolapse are not all the same, and that they should be screened for features associated with sudden cardiac death to help clarify their level of risk and possibly avoid a serious complication or tragic outcome. ■

We generally recommend exercise stress testing in patients with mitral valve prolapse and high-risk features

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