Sudden cardiac arrest and coexisting mitral valve prolapse: A case report and literature review

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Abstract

The aetiology of sudden cardiac arrest can often be identified to underlying cardiac pathology. Mitral valve prolapse is a relatively common valvular pathology with symptoms manifesting with increasing severity of mitral regurgitation. It is unusual for severe mitral regurgitation to be present without symptoms and there is growing evidence that this
subset of patients may be at increased risk of sudden cardiac arrest or death. The difficulty
lies in identifying those patients at risk and applying measures that are appropriate to
halting progression to cardiac arrest. This article examines the association of mitral valve
prolapse with cardiac arrests, the underlying pathophysiological process, and strategies for
identifying those at risk.

Case

A 45 year old male had a sudden collapse at home, witnessed by his partner who started
bystander cardiopulmonary resuscitation (CPR). His initial observed cardiac rhythm was
pulseless ventricular tachycardia (VT) on arrival of the emergency medical services. A direct
current shock was delivered resulting in asystole. The patient underwent a further 10
minutes of CPR prior to the return of spontaneous circulation, during which time
endotracheal intubation and positive pressure ventilation was commenced. The total low-
flow time was between 20-30 minutes. The patient was transported by air ambulance to a
tertiary cardiac arrest center. He was transferred to the accident and emergency
department where intravenous sedation was started and maintained. The body
temperature was measured at 34.9°C. Initial blood investigations were as follows: Troponin I
350 ng/ml, C-reactive protein < 4 mg/mL, leukocyte count 18 x 10^3/µL, sodium 140 mmol/l,
potassium 3.1 mmol/l, urea 6.6 mmol/l, Creatinine 66 micromol/l, glucose 12 mmol/l. Initial
arterial blood gas sampling demonstrated a pH of 7.31, PaCO₂ 6.41 kPa, PaO₂ 62.9 kPa, base
excess -1.7, lactate 3.0 mmol/l. The ECG showed sinus rhythm, there were no signs of
ischaemia and it fulfilled electrical criteria for left ventricular hypertrophy (figure 1). A chest
X-ray showed the presence of an endotracheal tube, but was otherwise unremarkable. A CT scan of the head was obtained which was reported as normal.

Figure 1. Initial ECG on admission to hospital

Collateral history determined that the patient had no significant co-morbidities and he was healthy prior to the sudden cardiac event. A bedside transthoracic echocardiogram (TTE) was obtained (see videos 1 and 2). This reported a thickened and prolapsing anterior mitral valve leaflet with associated severe mitral regurgitation (MR). The left ventricular ejection fraction (LVEF) was inappropriately normal, but not hyperdynamic - although impaired when the severe MR was taken into account. There was no evidence of a systolic regional wall motion abnormality. On this evidence the patient was treated empirically with vancomycin and gentamicin for suspected infective endocarditis and transferred to the Intensive Care Unit (ICU).

Video 1. Parasternal long axis TTE zoomed in on the mitral valve showing a prolapsing anterior leaflet with evidence of cordal rupture.

Video 2. Apical 2/3 chamber TTE zoomed in on the mitral valve showing the anterior leaflet.

In line with current protocols, the patient’s temperature was allowed to increase to 36°C and maintained at this level for the first 24 hours. An infusion of norepinephrine was commenced to maintain a mean arterial blood pressure greater than 65 mmHg. A transoesophageal echocardiography (TOE) was performed 12 hours after admission (see
videos 3 and 4). This confirmed a flail A2 segment secondary to chordal rupture with evidence of myxomatous degeneration. The mitral annulus was dilated at 5.2 cm. No vegetations were observed on the mitral valve. Doppler interrogation confirmed the presence of severe MR. The left ventricle (LV) diastolic dimension was 7.2 cm, systolic dimension 5.3 cm and ejection fraction (Simpson’s biplane) was 58%. A coronary angiogram was performed and showed normal unobstructed coronary arteries. Empirical antibiotic therapy for bacterial endocarditis was discontinued following TOE.

Video 3. TOE showing a truncated commissural view with a prolapsing A2 segment of the anterior leaflet.

Video 4. TOE showing the 2D appearance from Video 3 with colour flow doppler added. There is regurgitation through the centre of the valve corresponding to A2. This is difficult to visualise due to the hyperdynamic ventricular function.

Following antibiotic therapy for hospital acquired pneumonia, mechanical ventilation was successfully weaned and the trachea was successfully extubated one week after admission. Although the patient experienced an initial deficit of his short-term memory function he continues to make a good neurological recovery. Prior to hospital discharge, a single lead implantable cardiac defibrillator (ICD) was inserted given his significant risk of further malignant ventricular rhythms. Three weeks later, a cardiac magnetic resonance imaging scan (CMR) was performed, which showed a severely dilated left ventricle with mild impairment of left ventricular function and severe mitral regurgitation. Further inquiry revealed no family history of sudden cardiac death, cardiac disease or connective tissue
disorders. Genetic testing is yet to be performed. The patient was discharged home from hospital 3 weeks after admission with referral for cardiac surgery to repair the mitral valve prolapse.

**Review of sudden cardiac arrest with co-existing mitral valve prolapse**

**Introduction**

We report a case of out of hospital cardiac arrest (OOHCA) secondary to ventricular tachycardia (VT) likely related to mitral valve prolapse (MVP) and severe mitral regurgitation.

Sudden cardiac death (SCD) is an unexpected natural death from a cardiac cause within a short time period \(^{(1)}\). In most epidemiologic studies, this short period is defined within one hour from the onset of symptoms. UK data shows an incidence of SCD is 100,000 adults per year \(^{(2)}\). In the USA, it accounts for about 300,000 cases annually representing about 50% of mortality from cardiac causes \(^{(3)}\). The overall incidence is about 50-100:100,000 people per year. On average, the survival with good neurologic recovery after OOHCA is about 5-10% \(^{(4)}\). Due to the short time period from onset of symptoms to arrest, identification of the high risk population and prevention is the most effective strategy. Causes of SCD include coronary artery disease, cardiomyopathies, structural heart disease and primary
electrophysiologic abnormalities. In some patients the cause remains unclear and hence the term “idiopathic ventricular fibrillation” is used (4).

**Definition**

MVP is defined as displacement of mitral leaflet tissue into the left atrium past the mitral annular plane during systole (5). It was first described by Barlow in the 1960s as an auscultatory and cine-angiocardioigraphic phenomenon, prior to the availability of diagnostic echocardiography (6-8). Advances in echocardiography (e.g. TOE and three dimensional imaging) have made it possible for accurate diagnosis and quantification of mitral regurgitation (9).

**The role of echocardiography in mitral valve prolapse**

Echocardiography can be used for diagnosis, surveillance and assessment of interventions in mitral valve prolapse. Carpentier’s functional classification of mitral regurgitation described MVP (Type II classification) as an abnormality of leaflet motion, where one or several components of the valve protrude into the left atrium (LA) during ventricular systole. 2D echocardiography can be used to divide MVP into classical and non-classical criteria for diagnosis. Classical MVP describes >2 mm displacement of the mitral valve leaflets into the LA in long axis view during ventricular systole, with leaflet thickness of ≥5 mm. Non-classical MVP is leaflet displacement >2 mm with leaflet thickness <5 mm.
Classical MVP will either have a symmetrical or asymmetrical point of coaptation. Both leaflets tips meet at the same point on the mitral valve annulus in symmetrical MVP. Asymmetrical coaptation results in one leaflet being displaced towards the LA in relation to the other leaflet. Assymetric coaptation is more likely to deteriorate and develop flail prolapse and result in greater severity of MR. Flail segment or prolapse describes the presence of leaflet tips that turn outwards and point into the LA. Flail prolapse can involve a single segment, multiple segments, one leaflet or both leaflets (likely secondary to cordal rupture).

Both 2D TTE and TOE can be used to evaluate mitral valve morphology (Table 1). TOE will more reliably provide superior views across the LA window and should be considered in all cases of MVP assessment. The diagnosis of MVP using TTE should only be made in parasternal long-axis view and/ or the apical long axis view as the hyperbolic paraboloid shape of the mitral valve annulus can give a false positive diagnosis of MVP. In addition, a description of the leaflet thickness or redundancy, annular dilatation and chordal length should be included. Visual accuracy of mitral valve shape and deformity may be improved using 3D echocardiography techniques, especially for anterior leaflet or commissural involvement.

Table 1. TOE and TTE views required for assessing location of mitral valve prolapse

Doppler imaging is essential to determine severity of regurgitation. This should involve quantitative measures to determine disease progression, predict outcome and assess suitability for intervention. It is recommended that the color flow Doppler area should not
be used to quantify severity of MR. Where feasible the vena contracta or PISA (proximal isovelocity surface area) should be used as a measure of severity\textsuperscript{12}. Both the pulsed Doppler mitral to aortic TVI (time velocity integral) ratio and the systolic pulmonary flow reversal can be used as adjuncts to assist with quantifying severity of MR\textsuperscript{12}.

The downstream effects of MR, including LA dilatation, LV dilatation, LV dysfunction, pulmonary vein flow reversal, pulmonary hypertension, RV dilatation and tricuspid regurgitation will also help determine severity of MR. LV dilatation is a particularly important marker of progression in asymptomatic regurgitation, with monitoring of LV end systolic diameter used to suggest when surgical intervention may be indicated.

Intra-operatively 2D TOE and/or 3D TOE is recommended to assist surgical repair or replacement of the valve\textsuperscript{14}. 3D TOE has been shown to be more reliable than surgical inspection at accurately diagnosing the cleft like indentations of the posterior mitral valve leaflet of myxomatous mitral valve disease and aid repair\textsuperscript{15}. It is also important in percutaneous methods of mitral valve repair such as with MitraClip\textsuperscript{16}.

**Epidemiology**

According to recent figures, the MVP prevalence is 1-2.4\% \textsuperscript{(17, 18)}. This is down from previous estimations of up to 35\%. This difference can be explained by better understanding of the anatomy of the mitral valve, stricter diagnostic criteria and better diagnostic technology. Nevertheless, MVP remains the most common cause of mitral regurgitation in developed countries.
Pathophysiology of mitral valve prolapse

Several pathological processes may cause prolapse of the mitral valve including rheumatic heart disease, Marfan’s syndrome, endocarditis and myocardial ischemia but degenerative MVP refers specifically to a specific spectrum of primary lesions. On the two extremes of the spectrum are fibro-elastic deficiency (FED) and Barlow’s disease. FED is a fibrillin deficiency leading to rupture of one of the chordae. In this case the mitral valve leaflets are thinned and the annular size is normal. At the other end of the spectrum is Barlow’s disease affecting younger patients. The mitral annulus may become calcified and dilated with thickened leaflets secondary to myxomatous degeneration.

Arrhythmias

Both supraventricular (SVA) and ventricular arrhythmias (VA) are associated with complications of MVP. This high incidence rate has been recognised for more than 20 years. A study in 1994 reported an incidence of SVA and VA associated with MVP of 14% and 30% respectively. When tested with continuous ECG monitoring, MVP patients had a prevalence of VA as high as 34% with premature ventricular contractions as the most common pattern (66% of cases). Moderate to severe MR has been shown to be an independent risk factor to developing arrhythmias. Ikeda studied patients with idiopathic ventricular tachycardia, and found a high prevalence of MVP (12 out of 35 patients). VT originated from the LV in most of these cases in contrast to non-MVP (91.7% versus 69.6%). Abnormal ventricular repolarisation including early
repolarisation has also been linked to the presence of MVP\(^{24,25}\). A cross-sectional study of 100 patients with MVP showed a high incidence of early repolarisation (represented by notch in descending arm of QRS and J-point and/or ST segment changes) compared with healthy individuals without MVP\(^{25}\).

**Left ventricular remodeling**

The presence of a dilated left ventricle in the context of severe MR may indicate a period of LV remodeling. In acute primary MR afterload may initially decrease due to the alternate pathway for ejection. However, with volume loading of the LV over time the relatively thin walled LV may dilate and hypertrophy. Consequently the afterload in chronic compensated MR will be normal and elevated in chronic decompensated MR\(^{26}\). Remodeling of the LV may allow MR to be tolerated with mild or no symptoms by increasing stroke volume. On the other hand progression to heart failure and possibly cardiac arrest can occur rapidly often in the presence of myocyte dysfunction and sympathetic activation\(^{27}\). LV remodeling has been associated with evidence of ventricular arrhythmias. However, there is a paucity of evidence assessing this link in the context of mitral valve prolapse without coronary artery disease\(^{28}\).

**Incidence of sudden cardiac death**

Despite the general impression of a benign course, several case reports since the 1980’s describe SCD in MVP patients, with a significant proportion of young and previously asymptomatic individuals\(^{29,30}\). A debate continues as to whether MVP is the cause of SCD
or merely an association. Data from forensic autopsy examinations have reported floppy mitral valves in 5% of specimens (99 out of 2007 specimens). From those, MVP was considered directly responsible for the death of 17 patients (0.8% of cases)\(^{(31)}\). This would rank MVP as the most common congenital and valvular cardiac cause of SCD. A consensus statement in 1997 from American and European societies does not attribute the cause of SCD to MVP unless the prolapse is associated with valve redundancy, thickening and regurgitation, QT prolongation, or ST-T wave changes\(^{(32)}\).

It is not known if the mitral valve repair or replacement will have a preventive effect on ventricular arrhythmias. Subsequently, the American Heart Association/ European Society of Cardiology guidelines for ventricular arrhythmias and SCD have no distinctive recommendations for the management of VA or SCD in mitral valvular heart disease\(^{(33)}\). Moreover, neither the recent American nor European valvular heart disease guidelines mention a criterion for predicting or assuming SCD secondary to MVP\(^{(33, 34)}\).

The 10 year mortality of asymptomatic MVP patients is reported to be 19% with greater than moderate MR and impaired LV function as the most important risk factors\(^{(35)}\). This is not different from the all-cause mortality from MR with a flail leaflet (MR-FL). Collective data from all cause mortality from MR-FL showed an annual mortality of 1.8%. Not surprisingly, LVEF and NYHA class were the risk factors for mortality. However, in the subgroup of patients with SCD, 40% of patients were categorised as NYHA class 1\(^{(36)}\). This highlights a subgroup of patients with SCD predominantly due to cardiac arrhythmia and not related to the severity of MR or LV failure in MVP. These patients were mostly young and asymptomatic. The subgroup of patients with NYHA class I had a yearly risk of SCD of 1\%\(^{(36)}\).
This is equal to the overall mortality in hypertrophic obstructive cardiomyopathy (HCM). A pathology considered as one of the most common causes of SCD in young people \(^{[37]}\). Consequently, it is logical to identify a high risk group of MVP similar to the recommendation for primary prevention in HCM.

**Risk of sudden cardiac death**

As the incidence of SCD is very low in patients with MVP, studies have been directed towards identifying a high risk subgroup that could benefit from primary or secondary prevention. Autopsy evaluation of SCD patients associated with MVP, identified a subgroup of patients with isolated MVP. These patients were younger, mostly females and with less prevalence of MR \(^{[38]}\). The high prevalence of MVP makes a strategy based on primary prevention feasible if the high risk group could be strictly defined. Advances in echocardiography, CMR and electrophysiology are promising in the identification of this group. Currently, no clear strategy is recommended for this small subgroup. Being young and asymptomatic makes it difficult to detect patients for primary prevention. On the other hand we know that the incidence of SCD is much lower in young adults than the general population (i.e. about 1:100,000). This incidence doubles if athletic \(^{[39]}\). It is not known whether exercise increases the risk of SCD in MVP patients. Till now MVP associated SCD is categorised as idiopathic VF. The real question is whether it is possible to prospectively identify risk factors for SCD in individuals with MVP.

A retrospective American study identified 12 out of 50 SCD patients with idiopathic VF as having MVP. A quarter of MVP patients had a family history of SCD \(^{[40]}\). Another study by
Vohra et al in 1993 prospectively studied 7 patients with MVP associated with mild MR and normal LV function. All patients initially presented with syncope or OOHCA and the mean follow up period was 2.5 years. They had proven ventricular arrhythmias on Holter or electrophysiological study (EPS). Patients were treated with anti-arrhythmic pharmacotherapy, although with limited efficacy as there were two who suffered sudden death. Two patients underwent reparative surgery, but the arrhythmias were re-inducible on repeat EPS \(^{(41)}\). This is in contrast to another study where surgical correction had a protective effect \(^{(36)}\).

**Prevention of sudden cardiac death**

A cohort study that reviewed 24 patients who had idiopathic VF/VT OOHCA found echocardiographic evidence of bileaflet MVP in 10 patients (42\%). The author named it malignant bileaflet MVP. Those patients with MVP had higher incidence of ECG abnormalities and ventricular arrhythmias \(^{(42)}\). Electrolyte disturbances can be an aggravating factor contributing to the occurrence of ventricular arrhythmias and subsequently SCD \(^{(43)}\). Screening programs, technical availability (ECG, echocardiography) and cost remain obstacles for a wide application of primary prevention. Nevertheless if MVP had been detected accidentally or in a screening program (e.g. athletes or relatives of patients with SCD), it may be easier to reconsider recommending a strategy for those patients depending on clear risk criteria. On the other hand, an ICD is not without risk especially for young people. EPS, MRI and echocardiography may be helpful in identifying the right group.
Secondary prevention is an easier question. In patients diagnosed with idiopathic VF, ICD is a class I recommendation for survivors (44). A follow-up of 24 patients with OOHCA with VF/VT, showed patients with bileaflet MVP had a significantly better ICD appropriateness compared with non-MVP patients (80% versus 36%, p=0.04). However, this may had been affected by a longer follow up period in the MVP group (42).

Cardiac magnetic resonance imaging

The advent of CMR has shed further light on this condition. CMR has shown an association between MVP and papillary muscle fibrosis. In a study of 16 patients, 8 had a history of VA on previous Holter monitoring (couples of VPCs or non-sustained VT) and 63% of the MVP patients had papillary muscle fibrosis on late gadolinium enhancement (45). Basal LV hypertrophy is another abnormality which can be better detected by CMR in such patients. However, Its significance in cases of arrhythmias and SCD remains unknown (46).

Other causes of SCD with MVP

It should be noted that other possible mechanisms of cardiac arrest should not be ignored. Primary spontaneous chordal rupture is one of the recognised complications of MVP. This may cause acute MR and cardiogenic pulmonary oedema (47). Intra-myocardial small vessel disease has a known association with SCD (48). One of its variants, fibromuscular dysplasia, had been observed by pathologic examination more frequently in MVP than in the controls.
This variant of small vessel disease in MVP cases was associated with fibrosis of the basal inter-ventricular septum\(^{(49)}\).

**Conclusion**

In this case, the patient was previously asymptomatic and presented with an aborted SCD. Severe MR was demonstrated with echocardiography. The presence of a dilated LV at presentation and later on during CMR suggests chronic severe MR with extensive LV remodeling in the absence of symptoms. It is possible that the hemodynamic effects of the acute regurgitation may have caused syncope which progressed to a dysrhythmia and cardiac arrest due to reduced coronary flow. It is equally possible that there was a primary dysrhythmia associated with mitral valve prolapse or left ventricular remodeling. Early TOE and CMR are important, as is a greater understanding of the possible electrophysiological mechanisms of primary arrhythmogenesis.

**Declaration of interests**

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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References


9. Cheng TO, Wang XF, Zhang J, Xie MX. Recent advances in the echocardiographic


12. Recommendations for the echocardiographic assessment of native valvular
regurgitation: an executive summary from the European Association of
Cardiovascular Imaging Patrizio Lancellotti, Christophe Tribouilloy, Andreas
Hagendorff, Bogdan A. Popescu, Thor Edvardsen, Luc A. Pierard, Luigi Badano, Jose L.
Zamorano, On behalf of the Scientific Document Committee of the European
Association of Cardiovascular Imaging: Thor Edvardsen, Oliver Bruder, Bernard
Cosyns, Erwan Donal, Raluca Dulgheru, Maurizio Galderisi, Patrizio Lancellotti,
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Kristina Haugaa, Giovanni La Canna, Julien Magne, Edyta Plonska Eur Heart J
Cardiovasc Imaging Jul 2013, 14 (7) 611-644.

M, Parolari A, Zanobini M, Alamanni F. Head-to-head comparison of two- and three-
dimensional transthoracic and transesophageal echocardiography in the localization

14. La Canna G, Arendar I, Maisano F, Monaco F, Collu E, Benussi S, De Bonis M,
Castiglioni A, Alfieri O. Real-time three-dimensional trans-esophageal
echocardiography for assessment of mitral valve functional anatomy in patients with


Figure 1: Initial ECG on admission to hospital
Initial ECG on admission to hospital
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