ESC European Society of Cardiology

European Heart Journal - Case Reports (2024) **8**, ytae372
https://doi.org/10.1093/ehjcr/ytae372

CASE REPORT
Valvular heart disease

Case report: arrhythmic mitral valve prolapse syndrome—are risk factors underdiagnosed?

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Received 5 January 2024; revised 10 February 2024; accepted 23 July 2024; online publish-ahead-of-print 16 August 2024

Background Arrhythmic mitral valve prolapse syndrome (ARMV) is a recognized but underdiagnosed disease pattern. Risk factors for ARMV are established but not very well known, and the association of the structural abnormality with ventricular arrhythmias is incompletely understood.

Case summary Here, we present the case of a young man who presented at our hospital for radiofrequency catheter ablation and mitral valve surgery after two episodes of survived sudden cardiac arrest. We discuss the diagnostic and therapeutic strategies that were used. We shine light on the risk factors for ARMV and why early identification is crucial. We address the topic of primary prevention and its limitations. Finally, we discuss different treatment modalities for patients with ARMV.

Discussion More awareness for ARMV is crucial. A consensus statement on clinical management exists, but scientific gaps in prospective data for primary prevention need to be filled and there is a need for a better understanding of the pathogenesis of ARMV.

Keywords Case report • Mitral valve prolapse • Sudden cardiac death • Risk factors • Mitral annular disjunction • Ventricular arrhythmia • Mitral regurgitation

ESC curriculum 2.2 Echocardiography • 4.3 Mitral regurgitation • 5.6 Ventricular arrhythmia • 5.11 Cardiac resynchronization therapy devices • 7.5 Cardiac surgery

Learning points

- Awareness for the presence of mitral annular disjunction and for risk factors of arrhythmic mitral valve prolapse syndrome needs to be raised. Furthermore, a better understanding of the underlying pathogenesis of this syndrome is needed and treatment guidelines based on clinical studies need to be established.
- At the moment, the aim of surgery in patients with arrhythmic mitral valve syndrome is mainly a reduction of mitral regurgitation. Its relevance regarding the impact on ventricular arrhythmias needs to be further investigated.

Introduction

Mitral valve prolapse (MVP) is the most frequent form of mitral incompetence. Mitral annular disjunction (MAD) is a structural abnormality of the mitral annulus. It results in a separation between the atrial wall insertion of the posterior mitral valve leaflet and the ventricular myocardium. Mitral annular disjunction leads to mitral annulus hypermobility and is often associated with myxomatous mitral valve disease. The magnitude of disjunction appears to be correlated with the number of proleptic valve segments.[1] The prevalence of MAD varies in the literature, presumably due to different definitions and imaging modalities.[1–3] The reported prevalence in a hospital-based transthoracic echocardiography (TTE)

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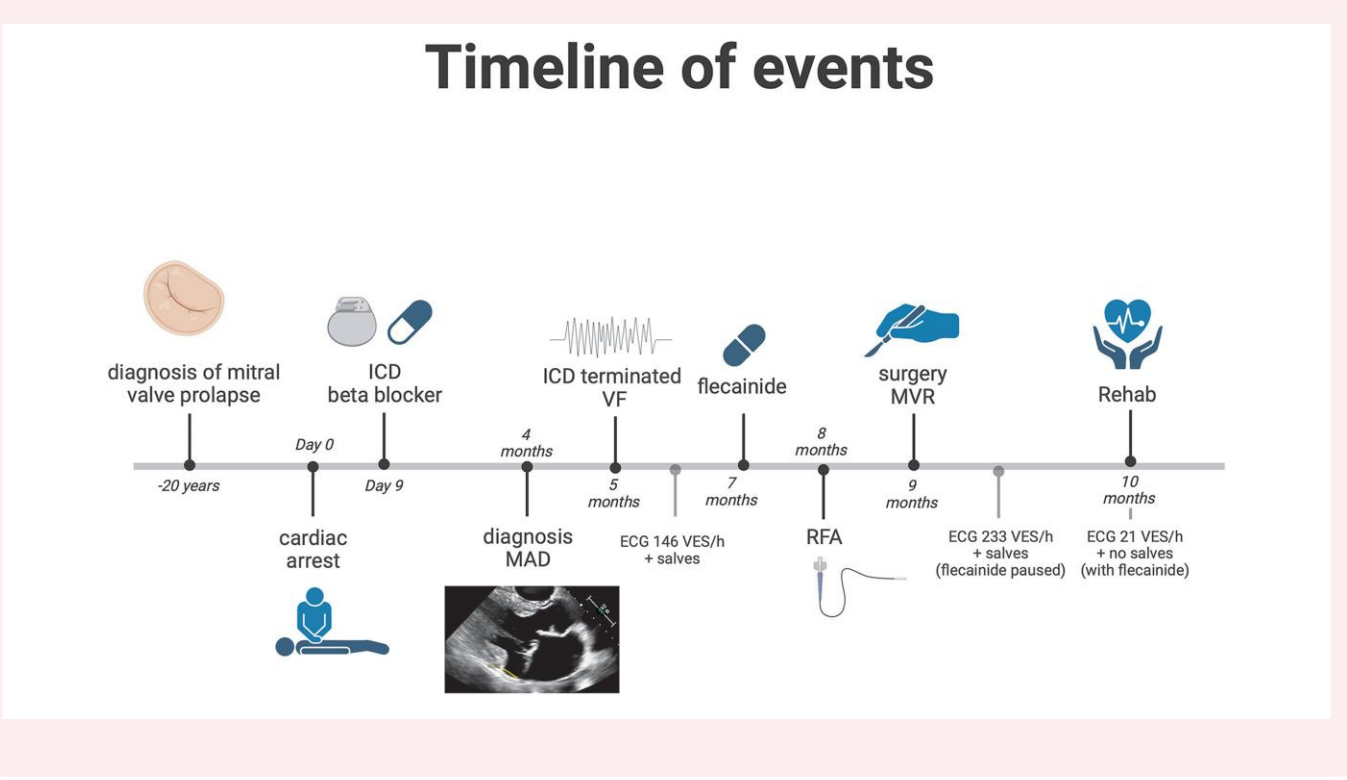
Handling Editor: Christoph Sinning
Peer-reviewers: Sebastian Feickert; Boldizsar Kovacs; henrike Aenne Katrin Hillmann
Compliance Editor: Nikesh Jathanna

cohort was 8.7%, with only 12% of the patients with MAD showing concomitant MVP.[2]

Arrhythmic mitral valve prolapse syndrome (ARMV) is defined by the presence of MVP (with or without MAD), combined with frequent and/or complex ventricular arrhythmias (VAs) in the absence of any other well-defined arrhythmogenic substrate.[4] In 2022, a consensus paper from the European Heart Rhythm Association was published, presenting the first guide on management of ARMV.[4] Still, standardized criteria from randomized trials regarding diagnosis, risk stratification, and management are missing. A couple of recent studies identified the following risk factors for ARMV: bi-leaflet prolapse, MAD, late gadolinium enhancement in magnetic resonance imaging (MRI), T-wave inversion in electrocardiogram (ECG), and a history of syncope.[5–9] The publication of the EHRA consensus paper shows that there is increasing awareness of the syndrome. Still, the goal must be that this awareness finds its way into the clinical routine, which is the aim of this case report.

Summary figure

Timeline of events—ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; MAD, mitral annular disjunction; MVR, mitral valve reconstruction; RFA, radiofrequency ablation; VF, ventricular fibrillation/tachycardia.



Case presentation

At the age of 38 years, a currently 39-year-old man experienced out-of-hospital cardiac arrest (CA) due to ventricular tachycardia (VT)/fibrillation, while physically active in a fitness centre. Immediate cardiopulmonary resuscitation and external defibrillation led to the return of spontaneous circulation and a favourable neurologic outcome. Upon hospitalization, computed tomography ruled out pulmonary embolism or aortic dissection. Initial physical examination was limited because the patient was intubated and sedated. Still, peripheral circulation was normal, the pupils were narrow, and the abdomen present unremarkable. A coronary angiography excluded coronary artery disease. In an electrophysiological study, a non-sustained polymorphic VT from the right ventricular apex could be induced and accessory pathways were ruled out. The TTE and transoesophageal echocardiography (TEE) showed moderate mitral regurgitation with a bi-leaflet MVP and thickened leaflets consistent with Barlow's disease. Ejection fraction (EF) was around 47% with mild global hypokinesia. An implantable cardioverter defibrillator (ICD) was implanted, and treatment with bisoprolol (2.5 mg daily dose) was initiated. A Holter ECG showed an intermittent ventricular bigeminus, and the ICD interrogation at 2 months confirmed a high ectopic burden but no sustained arrhythmic events.

The patient had been aware of the MVP for 20 years, which was evaluated once 10 years before CA without further consequences. There was no further medical history/medication at the time of presentation with CA. Signs of MAD are not mentioned in the hospital report but are described by the cardiologist who saw the patient 4 months after the CA for a check-up. There is no history of syncope, and the patient's family history is unremarkable for cardiac disorders.

During follow-up after the above-described index event, a TTE 4 months later revealed stable conditions, whereas an exercise stress ECG persistently showed sustained ventricular bigeminy and a few higher-grade non-sustained VAs.

Approximately 5 months after the CA, VT occurred and was terminated adequately by the ICD (*Figure 1*). Again, the incident happened while the patient was physically active. He was just getting into a pool and about to start swimming when he lost consciousness for a couple of seconds.

Seven months after CA, the patient was admitted to our clinic for further diagnostics and evaluation of treatment options. Implantable cardioverter defibrillator interrogation revealed numerous non-sustained VTs besides the above-mentioned sustained VT. Inferolateral T-wave

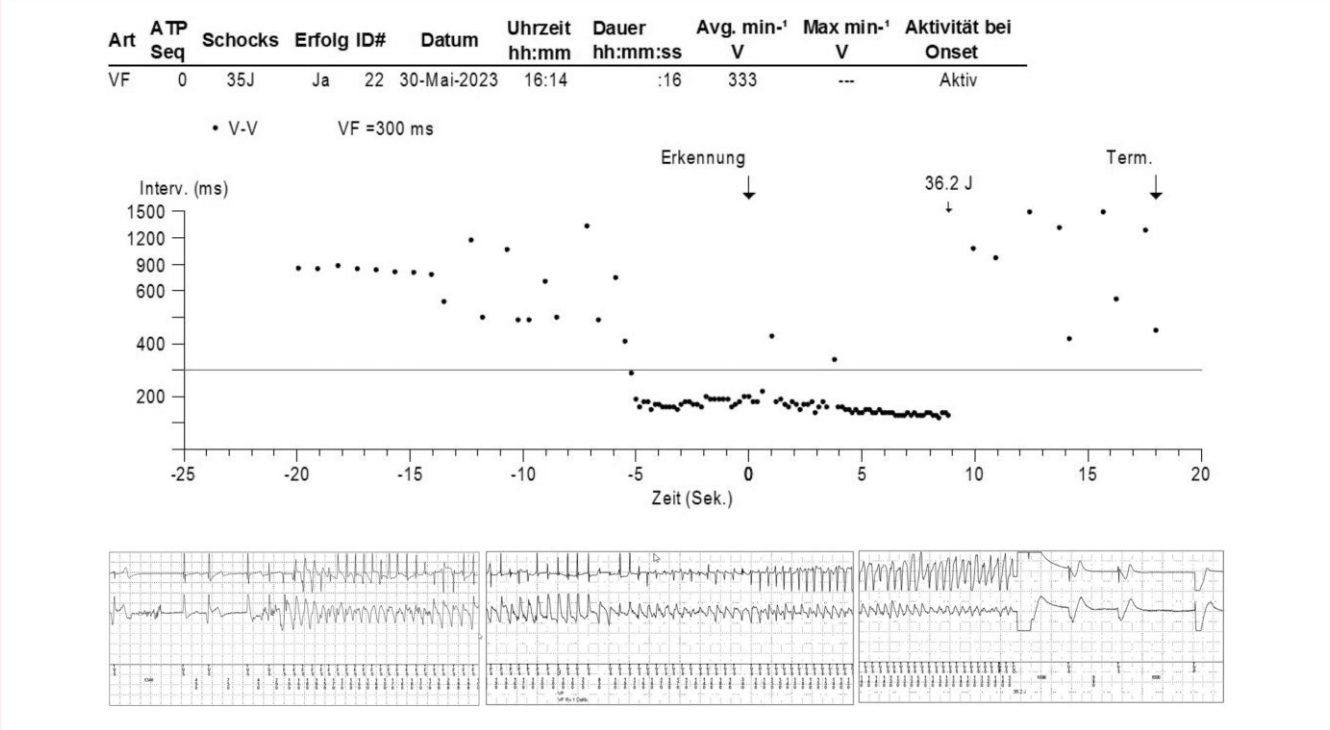


Figure 1 Implantable cardioverter defibrillator trackings of the ventricular tachycardia episode in May 2023 triggering a 36.2 J shock shown as plot (above) and as near-field and far-field electrogram (EGM) (below). This record clearly shows a polymorphic high-risk ventricular tachycardia.

inversions could be detected in the resting ECG. Holter ECG confirmed a disposition for VAs with an average of 146 ventricular ectopic beats per hour and eight non-sustained VT episodes, the longest lasting over 37 beats, under therapy with bisoprolol (2.5 mg daily dose). Subsequently, pharmacological therapy with flecainide (100 mg, every 12 h) was initiated. The TTE described a relevant dilatation of the left ventricle (63 mm end-diastolic diameter), a mildly reduced EF, moderate mitral regurgitation, and the previously described MAD. (*Figure 2* and Supplementary material). Subsequently, TEE unveiled severe mitral regurgitation and Barlow's disease (*Figure 3*). These findings were further confirmed by MRI. Magnetic resonance imaging-based cardiac fibrosis assessment by late gadolinium enhancement was unsuccessful due to ICD-related artefacts.

Upon completion of the diagnostic evaluation, the heart team consensus supported surgical therapy of the MVP, preceded by an attempt to reduce the burden of premature ventricular contractions (PVCs) using radiofrequency (RF) catheter ablation after cessation of flecainide.

High-resolution electroanatomic mapping using a multipolar mapping catheter (PentaRay, Biosense Webster) and the Carto 3 v7 navigation system (Biosense Webster) revealed ventricular ectopy originating from both the anterolateral mitral valve annulus and the anterolateral papillary muscle (*Figure 4*). Application of 50 W RF via an irrigated single-tip ablation catheter (SmartTouch SF, Biosense Webster) resulted in a significant suppression of ectopy. Importantly, the electrophysiological procedure was able to locate the arrhythmia and initially successfully treat the arrhythmia by RF application with no re-occurring PVC during a waiting period of 30 min. The procedure was then terminated under the impression of a successful outcome. However, the PVC re-occurred during follow-up. Therefore, flecainide was re-initiated.

Nine months after CA, the patient was admitted for mitral valve surgery. A minimally invasive approach was chosen. The mitral valve was reconstructed by performing a ring annuloplasty with a 42 mm ring (LivaNova). Additionally, the posterior leaflet was fixed with five Gore-Tex sutures (ONX Loops 12 mm). The surgery proceeded without complications, and the following intensive care unit therapy and in-patient recovery were unremarkable. Post-surgery TTE showed no apparent residual MAD, but a mildly reduced left ventricular EF remained (*Figure 2* and Supplementary material). The mitral valve showed minimal residual regurgitation. Flecainide therapy was continued after surgery as another Holter ECG demonstrated persistence of 233 ventricular ectopic beats per hour and 24 non-sustained runs (*Figure 5*). Subsequently, the patient was discharged in stable general conditions.

Short-term follow-up 4 weeks after surgery confirmed a patient presenting in good overall condition. Holter ECG on flecainide showed a residual persistence of 21 ventricular ectopic beats per hour and no VT. Another Holter ECG on flecainide 5 months after surgery showed even fewer ventricular ectopic beats (~2/h). The patient was feeling fine and did not report of any complaints. Further controls during long-term follow-up are advisable.

Discussion

Nowadays, ARMV is a recognized syndrome, but the association of the structural abnormalities with VAs is incompletely understood.

We present the case of a young patient with MVP and the following risk factors for ARMV: MAD, bi-leaflet prolapse, ventricular ectopy, and T-wave inversion. In this case, MAD was diagnosed more than 20 years after MVP, although it seems very likely that MAD has been present before. As *Figure 2* shows, MAD is easy to detect in TTE once the examiner is familiar with this anatomic condition and its further implications. Careful and alert echocardiographic examination of patients with MVP regarding the presence of MAD could help to identify the patients at risk for sudden CA in an early stage. Also, MRI is suited for risk

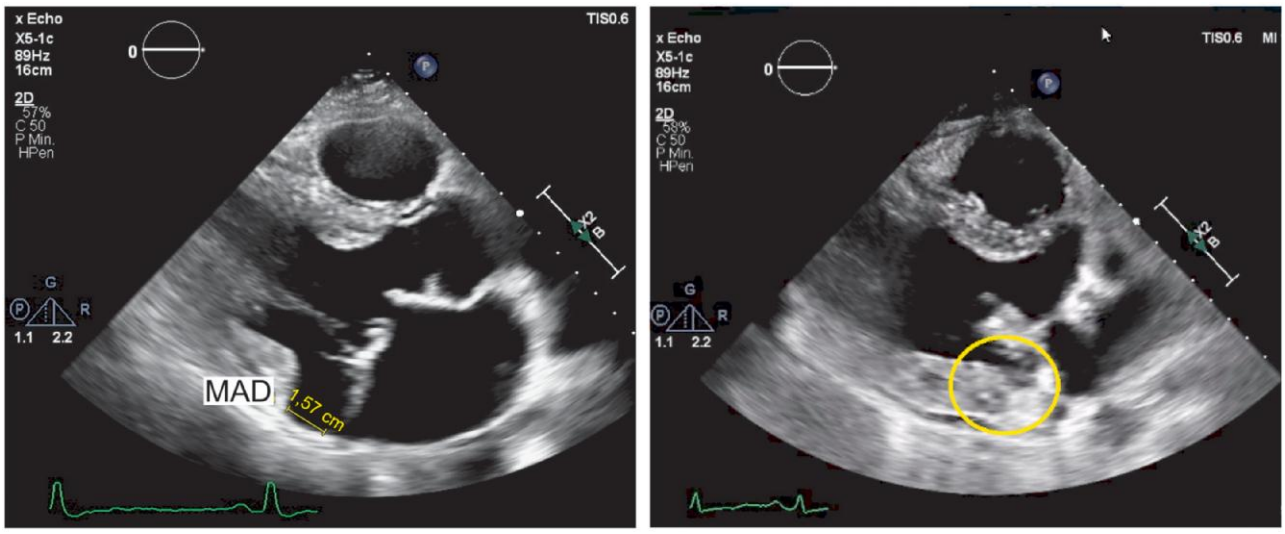


Figure 2 Transthoracic echocardiography image of mitral annular disjunction measuring 1.57 cm 7 months after cardiac arrest (left image) vs. transthoracic echocardiography image after surgery (right image). During surgery, the ventricular myocardium was lifted; mitral annular disjunction (supposedly within the circle) is not present anymore. MAD, mitral annular disjunction.

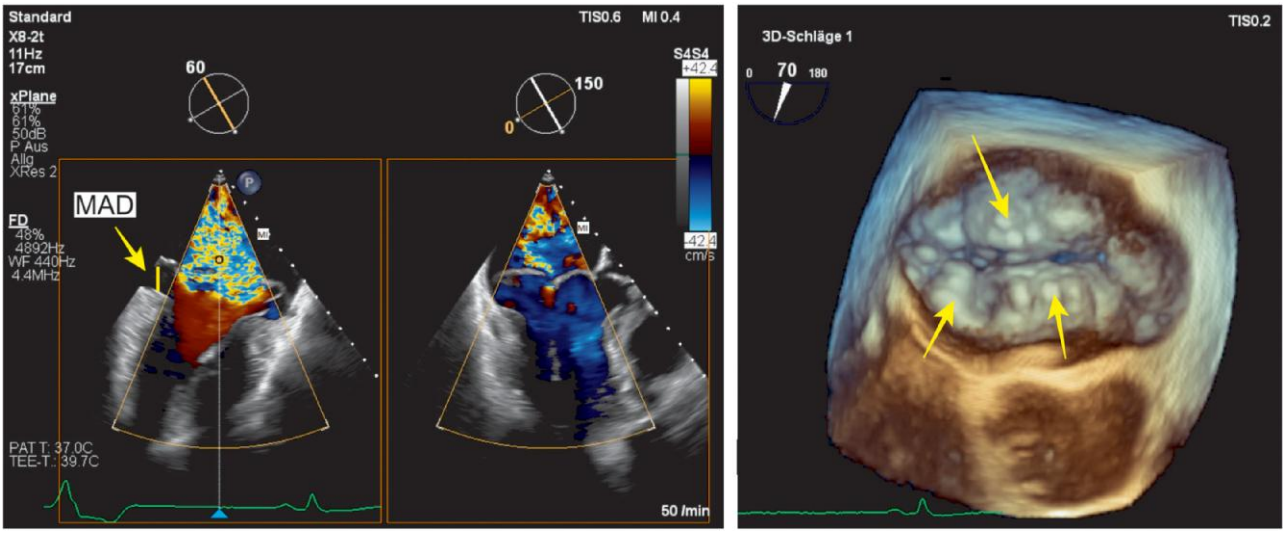


Figure 3 Transoesophageal echocardiography image showing mitral annular disjunction and mitral regurgitation (left image) as well as mitral valve prolapse (3D image on the right)—images used with kind permission from Dr Michael Mehr. MAD, mitral annular disjunction.

stratification of VAs in patients with MVP[4] and could have supported the patient's risk assessment if conducted before the CA. What would have been the consequences for our patient?

It might be speculated that the first CA could have been avoided by a comprehensive screening for arrhythmias.

However, the EHRA consensus paper recommends an ICD only after the detection of a high-risk VT or after aborted CA.[4] Interestingly, the recommendation for ablation and/or antiarrhythmic drugs (AADs) is also linked to the precondition of an aborted CA. This might arise from the fact that a typical focus of ARMV-related VAs is the papillary muscle, which is often very difficult to reach for ablation.

A case series published in 2022 describes a reduction of VAs after initiating flecainide therapy on top of low-dose beta-blockers in patients with ARMV.[10] Our case report suggests a similar tendency. Still, randomized controlled trials on the use of flecainide in ARMV patients are needed before standardized clinical implementation of flecainide. The writing group raises the question, of whether AAD should be recommended earlier in cases with high VA burden so that CA could potentially be avoided.

The EHRA consensus authors instead recommend the implantation of an implantable loop recorder (ILR) in case of the documentation of a non-high-risk VT, after a syncope or in the presence of multiple phenotypic

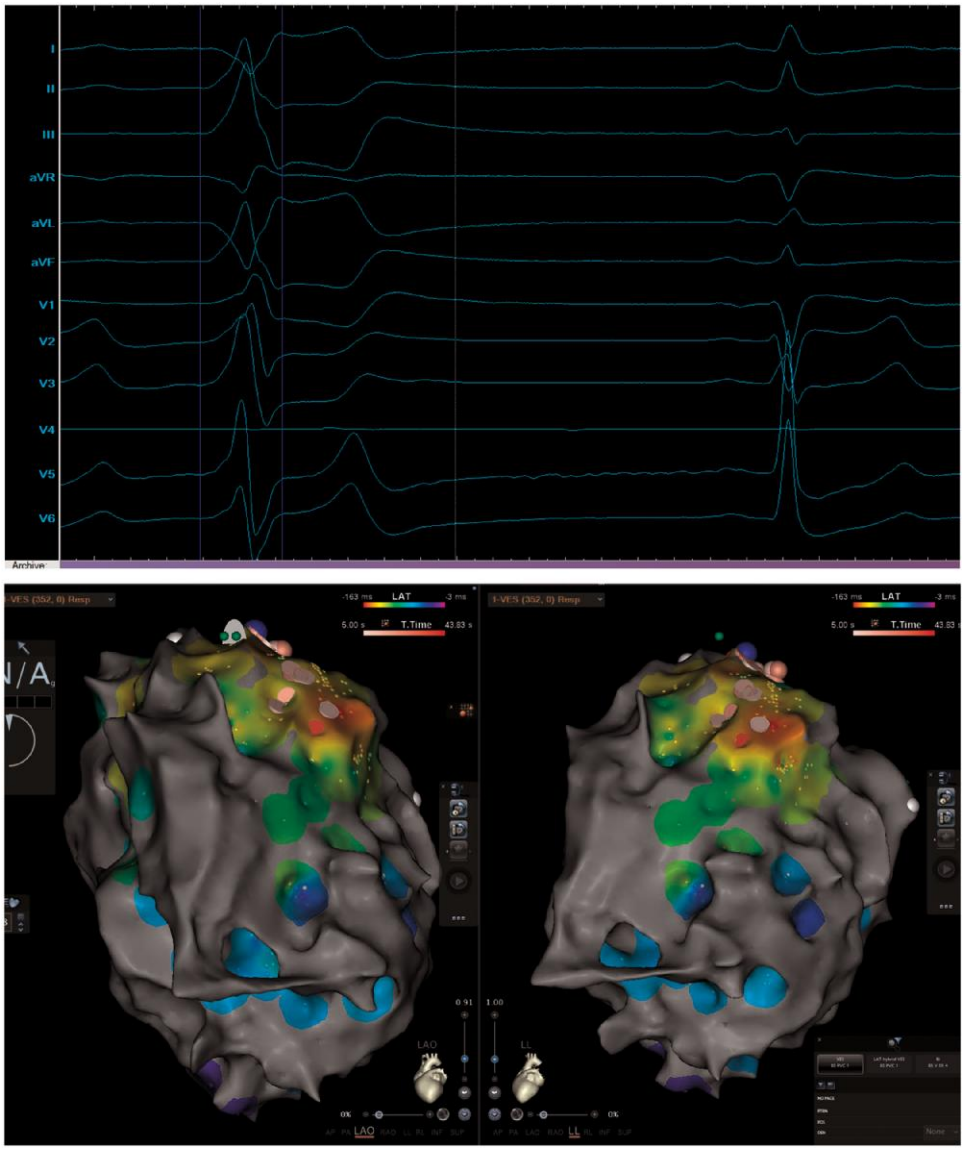


Figure 4 Above: electrocardiogram showing the targeted premature ventricular contraction (first beat) and the sinus beat (second beat). V4 shows an isoelectric line due to an accidental disconnection of the lead during the procedure. Below: high-resolution electroanatomic mapping showing ventricular ectopy originating from both the anterolateral mitral valve annulus and the anterolateral papillary muscle. Left anterior oblique (LAO) projection, left image; left lateral (LL) projection, right image.

risk factors (e.g. T-wave inversion in the inferior leads, MAD, and redundant MV leaflets). Our patient would have fulfilled various risk factors and therefore should have received at least an ILR (or in case of documentation of a high-risk VT an ICD). Unfortunately, no diagnostic Holter ECG was made in the 20 years between the diagnosis of MVP and the CA.

Considering that in real life, reimbursement after ILR implantation is often a problem and that an ILR is not able to trigger any therapeutic intervention in case of a VT, its mere benefit is the search for arrhythmia and, if applicable, the discrimination between high-risk VT and non-high-risk VT. We would rather prefer the earlier administration of AAD in patients with risk factors and a relevant VA burden to avoid the occurrence of syncope or CA beforehand.

The correction of MAD by mitral valve surgery may have a role in reducing VA burden, but data are inconsistent and mainly derived from case series. Also, not only VA reduction but also new-onset VAs have been described after surgery.[11] Our patient was not free of VAs after surgical correction. The indication for surgery was given by severe mitral regurgitation. Specifically designed studies are warranted to define the role of surgery in ARMV.

Also, genetic factors underlying ARMV are plausible. Several studies of families with ARMV have been conducted, and a couple of possible genetic targets have been detected.[12] At the moment, the EHRA consensus paper only suggests genetic testing in patients with syndromic disease (Marfan/Loeys–Dietz syndrome, etc.).[4] Until the submission of this report, the insurance company of our patient has not agreed to cover the costs of genetic testing. Official guidelines and multi-centre studies are needed to refine indications for genetic testing for future patients.

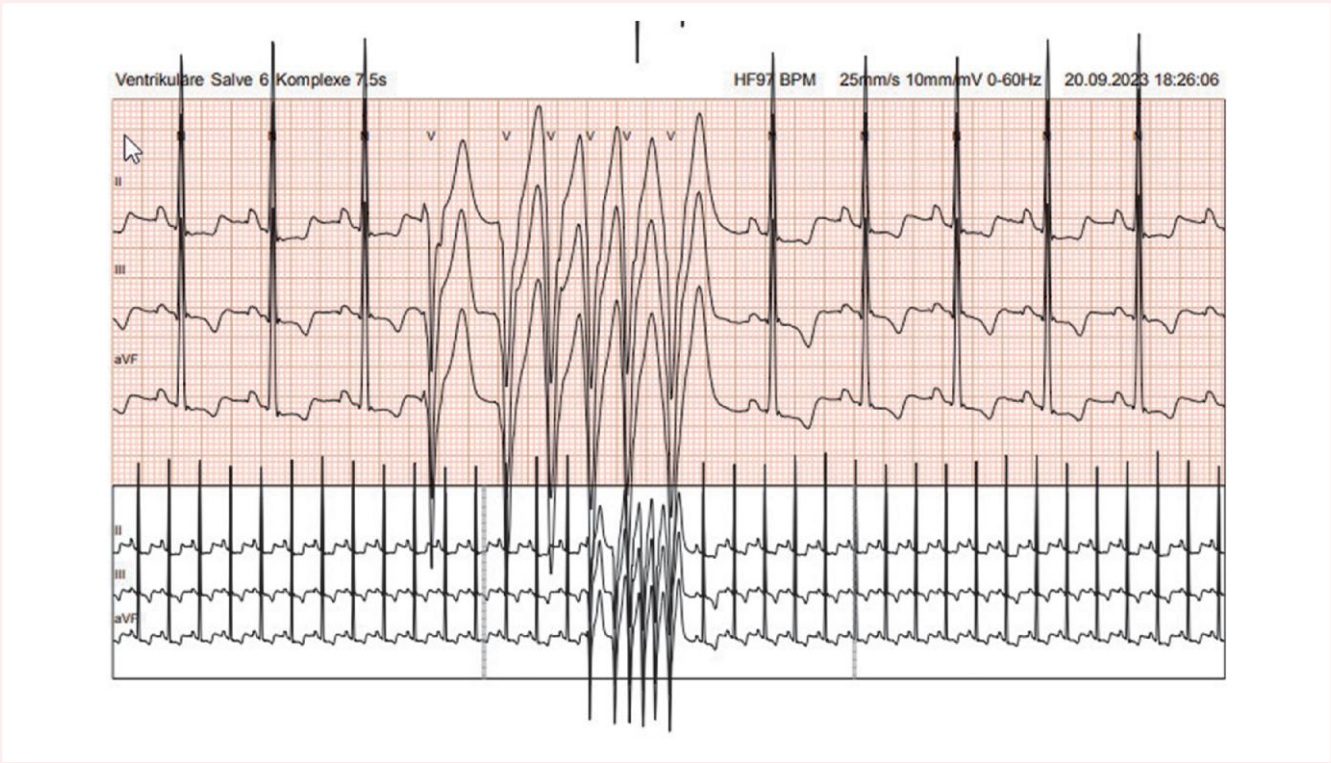


Figure 5 Holter electrocardiogram showing one out of 24 non-sustained runs post-operatively. Subsequently, flecainide therapy was resumed. Note the T-wave inversions in the inferolateral leads.

Conclusion

Mitral annular disjunction, bi-leaflet MVP, and VAs, among others, are important risk factors for ARMV. Awareness needs to be raised to increase their identification rate, and clinical decision-making for primary prevention needs to be supported by scientific guidelines established through randomized trials. We think that under certain circumstances, it is reasonable to initiate a treatment with AAD before CA, even if this is not supported by the current EHRA consensus statement.

Lead author biography

Dr Martina Steinmaurer is currently a cardiology resident with a background in cardiac surgery. She graduated from Ludwig Maximilian University in Munich. Her areas of interest include valvular heart disease, rheumatic heart disease, and cardiac imaging.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Acknowledgements

The authors would like to acknowledge the contribution of Dr Ahmad Ali, who performed crucial parts of mitral valve reconstruction, and the contribution of Dr. Stefan Müller, the patient's cardiologist, who was the first one to mention the MAD. They also express gratitude to all involved staff at the cardiology and cardiac surgery departments at LMU Hospital, Campus Großhadern.

Consent: The authors confirm that written consent for the submission and publication of this case report has been obtained from the patient following COPE guidance.

Conflict of interest: None declared.

Funding: The authors declare that this report did not receive any specific grant from funding agencies in the public, commercial, or non-profit sector.

Data availability

The data underlying in this article are available in the article and in its online supplementary material.

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