Myocardial fibrosis and sudden cardiac death (SCD) risk factors in mitral valve prolapse patients deemed to be at low SCD risk

J Doubell,[1] A Doubell,[1] J Steyn,[2] M Talle,[1,3] M Rajah[1] and P Herbst[1]

[1] Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa
[2] Division of Cardiology, Tygerberg Hospital, Cape Town, South Africa
[3] Department of Medicine, Faculty of Clinical Sciences, College of Medical Sciences, University of Maiduguri and University of Maiduguri Teaching Hospital, Maiduguri, Nigeria

Address for correspondence:
Jacques Doubell
Division of Cardiology
Tygerberg Hospital
Francie Van Zijl Drive
Cape Town
7500
South Africa

Email:
jacquesdoubell1@gmail.com

J Doubell https://orcid.org/0000-0002-5440-6917
A Doubell https://orcid.org/0009-0005-7699-8684
J Steyn https://orcid.org/0009-0005-0373-7694
M Talle https://orcid.org/0000-0001-8989-4941
M Rajah https://orcid.org/0000-0001-5599-6608
P Herbst https://orcid.org/0000-0002-7111-1993
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ABSTRACT

Introduction: Mitral valve prolapse (MVP) is associated with risk for sudden cardiac death (SCD); however, there is no consensus regarding risk stratification. Myocardial fibrosis is a substrate for SCD in these patients. Risk markers described for SCD are T wave inversion in the inferior leads and complex ventricular ectopy (ventricular couplets, non-sustained ventricular tachycardia [NSVT], and polymorphic ventricular ectopy), spiked configuration of the lateral annular velocities (Pickelhaube sign), and mitral annular disjunction (MAD).
Purpose: We aimed to investigate the prevalence of these risk factors in our population of MVP patients, a cohort clinically assessed as low risk for SCD. Furthermore, we aimed to investigate the association between these risk factors and myocardial fibrosis and to describe its pattern.
Methods: Our echocardiography database was reviewed from 1 October 2020 to 31 December 2021 for patients with MVP. Patients newly diagnosed from 1 July 2021 to 31 March 2023 were also enrolled. Investigations included a clinical evaluation, assessment for SCD risk markers with electrocardiography (ECG), a 48-hour Holter ECG, a transthoracic echocardiogram, and an assessment for myocardial fibrosis with cardiovascular magnetic resonance (CMR) imaging.
Results: A total of 39 patients, deemed to be at low SCD risk, without prior severe mitral regurgitation, malignant arrhythmias, cardiogenic syncope, or survived SCD, were included for analysis. Of the patients, 66% had areas of replacement fibrosis detected by late gadolinium enhancement (LGE). Segments commonly involved included the basal posterior (39%), basal inferior (39%), and basal lateral (25%). Areas involved were focal, with an average of 1.3 segments involved (± 1.3). No patient had diffuse fibrosis as assessed by extracellular volume (ECV) expansion. Known risk factors in our cohort included inferior T wave inversion (10%), polymorphic ventricular ectopy (18%), NSVT (16%), MAD (49%), and Pickelhaube sign (15%). No correlation was found between replacement fibrosis and any SCD risk marker.
Conclusion: Replacement fibrosis and SCD risk markers were common in this cohort, which was considered low SCD risk. No association was found between fibrosis and risk markers, suggesting poor predictive power for fibrosis. Risk markers for SCD are described in preselected, high-risk MVP populations. The extent to which these risk markers reflect SCD risk in low-risk patients is unclear. Using these risk markers in clinically low-risk patients may over-assess the risk, potentially resulting in medicalising patients and inappropriate therapy.
Keywords: mitral valve prolapse, sudden cardiac death, sudden cardiac arrest, myocardial fibrosis.
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INTRODUCTION

MVP is common, with 1–3% of the world's population being affected.[1] In the absence of severe mitral regurgitation, mitral valve prolapse (MVP) was previously considered a benign condition. However, long-term follow-up studies identified associations with SCD, infective endocarditis, cerebrovascular events, and progressive mitral regurgitation.[2] Since these earlier descriptions, there is a growing body of evidence of MVP's association with sudden cardiac death (SCD).[3]

SCD due to MVP is estimated to occur at a rate of 217 events per 100 000 person-years.[3] While this represents a low

individual risk, the high prevalence of the condition translates to a large total number of patients that may be affected. Identifying which patients with MVP are at higher risk of SCD (so-called malignant or arrhythmogenic MVP), and who would benefit from more intensive investigation, surveillance, and/or intervention to prevent SCD, is an important clinical question yet to be answered and an area of ongoing research. However, given the high prevalence of MVP and the fact that most patients have a low risk of SCD, the risk of over-investigation and medicalising these patients should be guarded against.

Identifying patients at high risk of SCD is challenging, and no reliable risk-stratification tool is currently available. Several risk factors for SCD in patients with MVP have been identified[1,3-5,6-9]:

- Electrocardiographic: T wave inversion in the inferior leads and complex ventricular ectopy [pleomorphic ectopic beats, ectopic couplets, or non-sustained ventricular tahcycardia (NSVT)].
- Echocardiographic: spiked configuration of the lateral annular velocities (Pickelhaube sign).
- Morphological: mitral annular dysjunction (MAD), posterior basal hypertrophy, and bileaflet prolapse.

The mechanisms linking these risk factors to SCD require further investigation, but it is postulated that they serve as risk markers for myocardial fibrosis, a substrate for arrhythmogenesis[10-12]. The identification of risk factors has largely been described in SCD survivors or patients with documented ventricular arrhythmia and has not been properly investigated in low-risk individuals. We aimed to investigate the prevalence of these risk factors in our population of MVP patients, a cohort clinically assessed as low risk for SCD. Furthermore, we aimed to investigate the association between these risk factors and myocardial fibrosis and to describe its pattern.

METHODS

The echocardiography database at Tygerberg Hospital was searched from 1 October 2020 to 31 December 2021 for patients with a MVP diagnosis. Patients identified via this database were contacted for possible enrolment. Patients presenting to Tygerberg Hospital's cardiology unit or surrounding referral centres with newly diagnosed MVP from 1 July 2021 to 31 March 2023 were also enrolled. Informed consent was obtained by the principal investigator. If necessary, an interpreter was provided. The study was approved by the Health Research Ethics Committee of Stellenbosch University (reference number: S21/02/017).

The inclusion criteria were patients with MVP (defined by superior displacement of the mitral leaflets > 2 mm beyond the mitral valve annular plane during systole), as assessed in a para-sternal long-axis view on a transthoracic echocardiogram.[1,13] The exclusion criteria were patients with severe mitral regurgitation, prior valve surgery, ischaemic heart disease, concomitant valvular or myocardial disease, and prior malignant arrhythmic events (ventricular tachycardia, ventricular fibrillation, or survived SCD).

Investigations performed in potential participants included a history and clinical examination, resting 12-lead ECG, 5-day Holter ECG, transthoracic echocardiography, and cardiovascular magnetic resonance (CMR) imaging. Patient demographic data, history, physical examination, and ECG and Holter ECG results were captured on a data collection form. Transthoracic echocardiography and CMR findings were performed using standard protocols (see below), and findings were reported on standard hospital reporting forms. All assessments were completed within 1 week of study enrolment.

Echocardiography

All patients underwent a comprehensive structural and functional two-dimensional (2D) transthoracic echocardiographic analysis performed on a General Electric (GE) machine (E95 scanner, GE HealthCare, Chicago, United States) with a standard 2D transducer (M5Sc 1.7–3.3 MHz) set to 2.5 MHz. A clinician experienced in echocardiography acquired and analysed the images, which the principal investigator then reviewed. All measurements were done in accordance with the British Society of Echocardiography guidelines for the acquisition of a minimum dataset required to define normality.[14] Standard atrial, ventricular, and valvular morphological and functional parameters were reported. In addition, a detailed mitral valve assessment was done with a view to defining MVP, describing the extent of prolapse (utilising Carpentier's segmental mitral valve model), and assessing current known risk predictors of SCD in MVP.[15]

Cardiovascular magnetic resonance imaging

Comprehensive CMR was performed at 1.5 Tesla, in accordance with consensus guidelines.[16-19] Standard long-axis views, as well as a stack of breath-held, retrospectively gated, steady-state free precession short-axis cine images, were obtained. Analysis was carried out using commercially available software (CMR42, Circle Cardiovascular Imaging, Calgary, Canada). Endocardial and epicardial left ventricular borders were traced in the short axis at end-diastole and end-systole to determine left ventricular volume, mass, and functional parameters. Papillary muscles were excluded from the blood pool. Quantitative analysis of short-tau inversion-recovery (STIR) images was performed following endo- and epicardial contouring in the short axis. A skeletal muscle (serratus anterior) region of interest was manually drawn in the same slice. Pre- and post-contrast T1 and pre-contrast T2 mapping images were obtained, the former using a shortened modified Look-Locker inversion sequence.

Late gadolinium enhancement (LGE) images were obtained with a T1-weighted, segmented inversion-recovery sequence at least 12 minutes after contrast administration. The location and distribution of myocardial fibrosis were determined. A standardised 16-segment model of the left ventricle was used to describe the distribution of identified abnormalities, as outlined by the American Heart Association.[20] Participants received Gadovist© contrast at the recommended dose of 0.2 ml/kg. MAD was reported if there was any degree of atrialisation of a mitral valve leaflet's annular hinge point, at any point around the

annulus. The degree and position of maximal disjunction (separation distance between the atrialised hinge point and ventricular myocardium) were then measured and reported.

STATISTICAL ANALYSIS

Statistical analysis was performed in consultation with Stellenbosch University's Division of Epidemiology and Biostatistics. Data were collected and recorded using an Excel spreadsheet and standard hospital reporting forms. The data were then imported into IBM SPSS Statistics version 28.0. (IBM, Armonk, United States) for statistical analysis. Standard descriptive statistics were used to analyse means, standard deviations (SD), medians, proportions, and frequencies. For quantitatively measured, high-risk clinical parameters, the data were tested for normality. Normally distributed data were expressed as mean ± SD. For categorical, high-risk clinical parameters, and to assess the association between myocardial fibrosis and risk factors, chi-squared tests or Fisher's exact two-sided tests were used as appropriate at the 0.05 level of statistical significance.

RESULTS

The initial inclusion criteria for MVP were met by 45 patients. Based on the exclusion criteria, 6 patients were excluded from analysis: 1 did not meet MVP criteria on expert review, 3 had severe mitral regurgitation, 1 had coronary artery disease with a previous myocardial infarct, and 1 withdrew consent due to claustrophobia, precluding CMR performance. The final number of patients included for analysis was 39. Data capture was incomplete for the group as a whole: 3 patients had uninterpretable Holter ECG results due to poor-quality recordings, 3 patients did not have CMR imaging, 2 due to claustrophobia, and 1 due to pregnancy, precluding gadolinium administration.

TABLE I: Patient demographics.

Demographics	***n* (%)**
Female	14 (33)
Age	41 ± 18
Age at diagnosis	31 ± 19
Race	
Caucasian	16 (41)
Black	4 (10)
Mixed race	19 (49)
Asian	0 (0)
Comorbidities	
Hypertension	6 (15)
Dyslipidaemia	5 (13)
Anxiety	7 (15)
Palpitations	26 (66)
Family history of MVP	3 (8)
Family history of SCD	0 (0)

MVP: mitral valve prolapse, SCD: sudden cardiac death.

Of the patients, 14 (33%) were female. The mean patient age was 41 years (± 18 years). Table I shows additional demographic information. Mean left ventricular end-diastolic diameter (LVEDD) was normal, measuring 4.9 cm (± 0.66 cm), and

TABLE II: Morphological and functional parameters assessed on cardiovascular magnetic resonance imaging.

	Mean	**Standard deviation**
Left ventricle		
LVEDD (mm)	48.34	6.45
PWT (mm)	10.41	1.91
IVS (mm)	10.59	1.73
LVEDV (ml)	186.69	63.21
LVEDVi (ml/m^2)	99.49	29.03
LVESV (ml)	75.19	26.47
LVESVi (ml/m^2)	41.10	13.03
LVSV (ml)	108.99	44.37
LVEF (%)	59.88	8.27
LV mass (g)	120.12	33.09
LV mass indexed (g/m^2)	65.33	14.35
Right ventricle		
RVEDD (mm)	43.94	5.19
RVOT (mm)	27.80	6.26
RV base to apex (mm)	86.87	10.67
RVEDV (ml)	179.56	56.80
RVEDVi (ml/m^2)	95.69	27.61
RVESV (ml)	85.10	41.63
RVESVi (ml/m^2)	44.34	21.10
RVSV (ml)	94.50	26.78
RVEF (%)	55.17	8.26
Left atrium		
LA diameter (mm)	31.33	8.50
Biplanar LA volume	85.62	73.75
LAVi (ml/m^2)	44.26	36.94
Right atrium		
Monoplanar RA volume	74.26	33.11
RAVi (ml/m^2)	43.04	20.18
Systolic MV annular diameter (mm)	37.08	6.67
Diastolic MV annular diameter (mm)	29.93	7.36
Mitral regurgitation		
Regurgitant volume (ml)	20.37	22.54
Regurgitant fraction (%)	20.17	17.83

IVS: Interventricular septum, LA: left atrium, LAVi: indexed left atrium volume, LV: left ventricle, LVEDD: left ventricular end-diastolic diameter, LVEDV: left ventricular end-diastolic volume, LVEDVi: indexed left ventricular end-diastolic volume, LVEF: left ventricular ejection fraction, LVESV: left ventricular end-systolic volume, LVESVi: indexed left ventricular end-systolic volume, LVSV: left ventricular systolic volume, MV: mitral valve, PWT: Posterior wall thickness , RA: right atrium, RAVi: indexed right atrium volume, RV: right ventricle, RVEDD: right ventricular end-diastolic diameter, RVEDV: right ventricular end-diastolic volume, RVEDVi: indexed right ventricular end-diastolic volume, RVEF: right ventricular ejection fraction, RVESV: right ventricular end-systolic volume, RVESVi: indexed right ventricular end-systolic volume, RVOT: Right ventricular outflow tract , RVSV: right ventricular systolic volume.

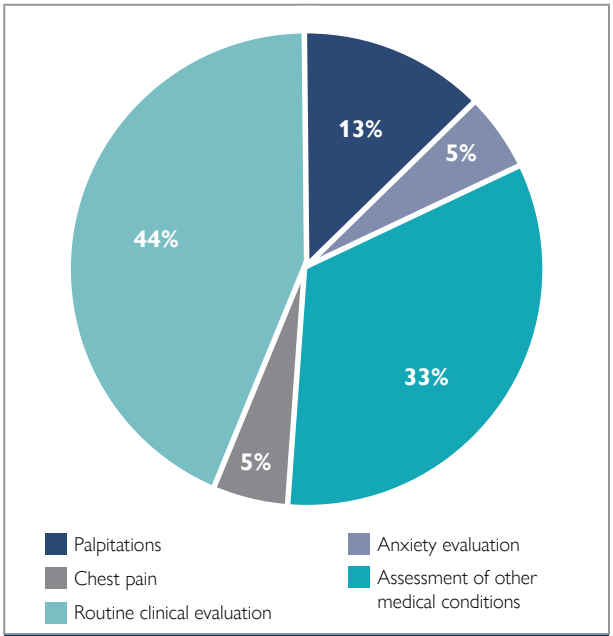

FIGURE 1: Presentations leading to mitral valve prolapse diagnosis.

indexed left ventricular end-diastolic volume (LVEDVi) measured 103 ml/m^2 (± 32 ml/m^2). The mean left ventricular ejection fraction was 60% (± 8%) (Table II).

Bileaflet MVP was present in 26 patients (70%). The frequency of the individual mitral valve segments involved in prolapse included: A1 (29%), P1 (42%), A2 (38%), P2 (86%), A3 (51%), and P3 (58%). Of the patients, 33 (89%) had associated mitral regurgitation, with a mean regurgitant volume of 21 ml (± 23 ml), in keeping with mild-to-moderate mitral regurgitation. Ventricular morphological and functional assessments were all made on CMR imaging.

No patient had documented survived SCD, sustained ventricular arrhythmia, or high-risk cardiac syncope. The MVP diagnosis was often incidental, with benign initial presentations (Figure 1). A history of palpitations was present in 26 patients (66%), and 21 (80%) described frequent palpitations. On further enquiry, 6 patients (15%) spontaneously offered a diagnosis of anxiety.

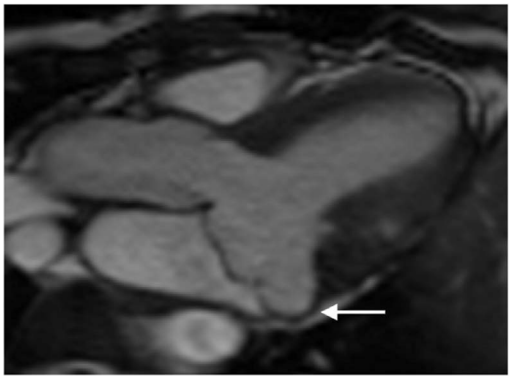

FIGURE 2: Long-axis view demonstrating mitral annular disjunction (arrow) of the posterior mitral valve annulus.

T wave inversion was noted in 4 patients (10%) on standard 12-lead ECG. The 5-day Holter ECG assessment demonstrated ventricular couplets in 22 patients (61%), pleiomorphic ectopic beats in 7 (19%), and NSVT in 6 (17%). Echocardiography demonstrated MAD in 24 patients (62%) (Figure 2) and Pickelhaube sign in 6 patients (15%). MAD was also documented in 24 patients (62%) on CMR, with a 6.6 mm (± 3 mm) mean MAD distance, basal posterior left ventricular hypertrophy (LVH) in 14 patients (38%), and basal lateral LVH in 11 patients (29%).

Myocardial replacement fibrosis was detected on LGE in 24 patients (66%) (Figure 3). The myocardial segments most commonly involved were basal posterior (39%), basal inferior (39%), and basal lateral (25%) (Figure 4). Replacement fibrosis tended to be focal, with an average of 1.3 segments (± 1.3) involved. No patients demonstrated diffuse fibrosis as assessed by ECV expansion (mean 25% ± 2%).

No association was found between any risk factor or combination of risk factors and the presence or absence of LGE (Table III). No association was found between bileaflet prolapse and segmental prolapse or arrhythmic profile.

TABLE III: Association between sudden cardiac death risk factors and late gadolinium enhancement*.

Sudden cardiac death RF	LGE positive		LGE negative		*p*-value
	RF present % (*n*)	RF absent % (*n*)	RF present % (*n*)	RF absent % (*n*)	
TWI	13 (3)	87 (20)	8 (1)	92 (12)	1.000
Ventricular couplets	67 (14)	33 (7)	58 (7)	42 (5)	0.716
Pleomorphic ectopy	19 (4)	81 (17)	25 (3)	75 (9)	0.630
Non-sustained VT	24 (5)	76 (16)	8 (1)	92 (11)	0.379
MAD	65 (15)	35 (8)	69 (9)	31 (4)	1.000
Basal hypertrophy	35 (23)	65 (15)	42 (5)	58 (7)	0.726
Pickelhaube sign	22 (5)	78 (18)	8 (1)	92 (12)	0.385

** Data capture was incomplete for the whole group, as 3 patients had uninterpretable Holter ECG results, and 3 patients did not have a CMR.*

LGE: late gadolinium enhancement, MAD: mitral annular disjunction, RF: risk factor, TWI: T wave inversion, VT: ventricular tachycardia.

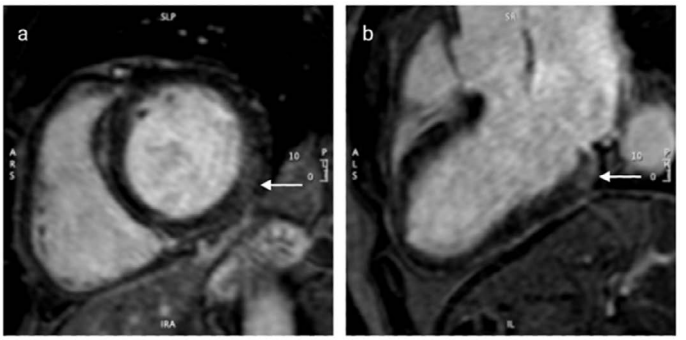

FIGURE 3: Phase-sensitive inversion-recovery images demonstrating late gadolinium enhancement (LGE).
a: Short-axis view at the basal level showing posterior segment LGE (arrow). b: Corresponding long-axis 3-chamber view showing LGE in the basal posterior wall (arrow).

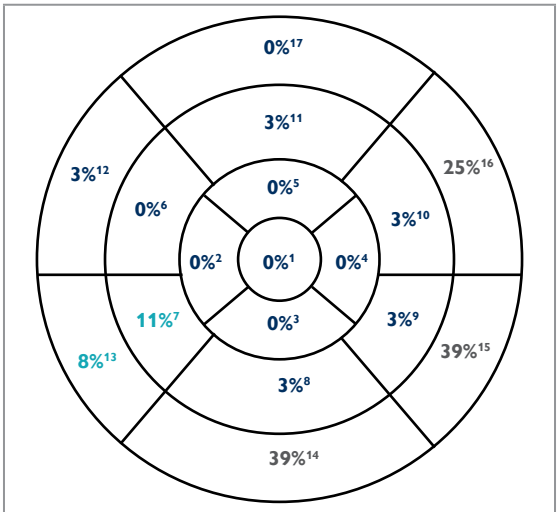

FIGURE 4: Percentage of patients with replacement fibrosis demonstrated on a left ventricular segmental modal.
1: apex 2, 2: apical septal, 3: apical inferior, 4: apical lateral, 5: apical anterior, 6: mid anterior septal, 7: mid inferior septal, 8: mid inferior, 9: mid posterior, 10: mid lateral, 11: mid anterior, 12: basal anterior septal, 13: basal inferior septal, 14: basal inferior, 15: basal posterior, 16: basal lateral, 17: basal anterior.

DISCUSSION

The absolute SCD risk in the general MVP population is considered low. Our cohort of otherwise healthy, community-based patients with no prior arrhythmic events and hitherto benign MVP mirrored the profile of a low SCD risk population. However, risk factors for SCD in MVP, as described in the literature, including focal replacement fibrosis thought to represent the arrhythmogenic substrate for arrhythmia and SCD in MVP, were common in this cohort. No correlation was found between replacement fibrosis and the described SCD risk factors. This highlights the need for further study in low-risk populations and a rational approach to SCD risk evaluation in MVP until more data are available.

Historical SCD cohorts have always attributed a proportion of community-based SCD to MVP.[21] It is important to understand that MVP was diagnosed on post-mortem studies and would therefore be expected to appear in SCD registries at a minimum frequency similar to that found in the background population. Subsequent scrutiny of this data demonstrated rates of SCD attributable to MVP that seemed to track the background prevalence closely, supporting MVP's initial status in the cardiology community as a benign condition.[2] This illustrates the problem of over-assessing risk when the background prevalence is not well known, which was a problem before the definition of MVP was revised, standardised, and incorporated into general echocardiography practice.[3]

Studies performed in high-risk SCD populations have identified an apparently high risk, or so-called malignant MVP cohort, with high SCD risk in a subset of MVP patients, which is supported by several subsequent publications.[1,3] The relatively high background prevalence of MVP appears to have hidden a small but definite incremental SCD risk attributable to MVP itself. Despite identifying a small, high-risk MVP cohort, it is important to remember that the absolute SCD risk in the general MVP population remains very low at an estimated 217 events per 100 000 person-years.[3] Unfortunately, this also means that any risk factor present at a high prevalence in the general low-risk MVP population is unlikely to be a very good predictor of SCD in the individual patient. Our study highlights this point of view.

When approaching SCD risk stratification of an individual with MVP using predefined risk factors, the positive and negative predictive values for SCD, and the pre-test probability for SCD related to the absolute prevalence of SCD in the population are critical metrics to consider. The low pre-test probability of SCD in the general MVP population makes it difficult to predict outcomes using commonly found risk factors.[3] The high baseline prevalence of currently used risk factors in MVP in our otherwise low SCD risk cohort underlines this problem. Furthermore, the identification of a high prevalence of replacement fibrosis, the putative mechanism underlying SCD in this population, and its lack of correlation with risk factors suggest that a more complex interplay of factors would need to be present to increase risk, again making it difficult to ascribe risk to this finding alone. However, the burden of fibrosis in individual patients in the current study was very low.

The pathophysiology of fibrosis, its degree and distribution, its association with MAD, the degree of MAD, and how it relates to annular movement and function may all be important factors to consider when assessing SCD risk attributable to fibrosis. This is an area that requires more study, as minor degrees of fibrosis appear to be a benign finding in most patients. In the current study, no association was found between the presence or absence of any risk factor or combination of risk factors for the presence or absence of LGE on CMR (Table I). Therefore, these risk factors may be markers of risk for SCD unrelated to replacement fibrosis alone, or that the burden of fibrosis needs to be substantially larger to accrue risk.

Given the high population prevalence of MVP, a potentially large absolute number of patients are at risk of SCD. Identifying which

patients with MVP are truly at high risk and would benefit from more intensive investigation, surveillance, and intervention to prevent SCD is a common clinical dilemma. The currently used risk factors derive from high-risk populations, and it is unclear how they should be applied to lower-risk populations for risk stratification. No current consensus guidelines exist to inform management in this scenario.

The risk of medicalising otherwise healthy individuals with associated over-investigation is high in this population. Larger outcome studies are required to follow low-risk MVP cohorts over longer periods to better understand what drives their risk. Overly aggressive investigation with electrophysiological studies, primary prevention intracardiac defibrillators, and investigations and devices with their own associated morbidity and mortality, seems unnecessarily aggressive in this population.

While risk stratification for SCD and the presence of fibrosis and SCD risk is well established for hypertrophic, ischaemic, and dilated cardiomyopathy, we do not currently have the data to support risk-stratification tools with appropriate negative and positive predictive values to implement similar strategies in MVP.[22-24] Our study suggests that the currently described high-risk factors are also common in low-risk patients, with a subsequently poor positive predictive value for SCD. The authors' opinion is that terms such as "malignant" or "arrhythmogenic MVP" should be avoided when assessing patients with MVP who have not had an arrhythmogenic event.

Study limitations

The current study involves a relatively small cohort of patients and has no longitudinal follow-up to assess event rates in this apparently low-risk population. However, the high prevalence of apparently high-risk features for SCD in a healthy, community-based cohort of patients with a common condition, and the low risk of SCD overall in the general MVP population, support the assertion of a poor predictive value of individual risk markers for the general MVP population.

CONCLUSION

This study highlights the need for ongoing investigation in this area, with the hope of accurately risk-stratifying MVP patients for SCD risk in the future. Before this data is available, one should avoid implementing risk stratification tools, especially in patients at an apparent low risk.

Conflict of interest: none declared.

REFERENCES

1. Miller MA, Dukkipati SR, Turagam M, et al. Arrhythmic mitral valve prolapse: JACC review topic of the week. J Am Coll Cardiol 2018;72(23 Pt A):2904-14. https://doi.org/10.1016/j.jacc.2018.09.048.
2. Nishimura RA, McGoon MD, Shub C, et al. Echocardiographically documented mitral-valve prolapse - Long-term follow-up of 237 patients. N Engl J Med 1985;313(21):1305-9. https://doi.org/10.1056/NEJM198511213132101.
3. Han H-C, Ha FJ, Teh AW, et al. Mitral valve prolapse and sudden cardiac death: A systematic review. J Am Heart Assoc 2018;7(23):e010584. https://doi.org/10.1161/JAHA.118.010584.
4. Sriram CS, Syed FF, Ferguson ME, et al. Malignant bileaflet mitral valve prolapse syndrome in patients with otherwise idiopathic out-of-hospital cardiac arrest. J Am Coll Cardiol 2013;62(3):222-30. https://doi.org/10.1016/j.jacc.2013.02.060.
5. Syed FF, Ackerman MJ, McLeod CJ, et al. Sites of successful ventricular fibrillation ablation in bileaflet mitral valve prolapse syndrome. Circ Arrhythm Electrophysiol 2016;9(5):e004005. https://doi.org/10.1161/CIRCEP.116.004005.
6. Basso C, Marra MP, Rizzo S, et al. Arrhythmic mitral valve prolapse and sudden cardiac death. Circulation 2015;132(7):556-66. https://doi.org/10.1161/CIRCULATIONAHA.115.016291.
7. Muthukumar L, Jahangir A, Jan MF, et al. Association between malignant mitral valve prolapse and sudden cardiac death: A review. JAMA Cardiol 2020;5(9):1053-61. https://doi.org/10.1001/jamacardio.2020.1412.
8. Marra MP, Basso C, De Lazzari M, et al. Morphofunctional abnormalities of mitral annulus and arrhythmic mitral valve prolapse. Circ Cardiovasc Imaging 2016;9(8):e005030. https://doi.org/10.1161/CIRCIMAGING.116.005030.
9. Ermakov S, Gulhar R, Lim L, et al. Left ventricular mechanical dispersion predicts arrhythmic risk in mitral valve prolapse. Heart 2019;105(14):1063-9. https://doi.org/10.1136/heartjnl-2018-314269.
10. Bui AH, Roujol S, Foppa M, et al. Diffuse myocardial fibrosis in patients with mitral valve prolapse and ventricular arrhythmia. Heart 2017;103(3):204-9. https://doi.org/10.1136/heartjnl-2016-309303.
11. Han Y, Peters DC, Salton CJ, et al. Cardiovascular magnetic resonance characterization of mitral valve prolapse. JACC Cardiovasc Imaging 2008;1(3):294-303. https://doi.org/10.1016/j.jcmg.2008.01.013.
12. Fulton BL, Liang JJ, Enriquez A, et al. Imaging characteristics of papillary muscle site of origin of ventricular arrhythmias in patients with mitral valve prolapse. J Cardiovasc Electrophysiol 2018;29(1):146-53. https://doi.org/10.1111/jce.13374.
13. Freed LA, Levy D, Levine RA, et al. Prevalence and clinical outcome of mitral-valve prolapse. N Engl J Med 1999;341(1):1-7. https://doi.org/10.1056/NEJM199907013410101.
14. Robinson S, Rana B, Oxborough D, et al. A practical guideline for performing a comprehensive transthoracic echocardiogram in adults: The British Society of Echocardiography minimum dataset. Echo Res Pract 2020;7(4):G59-G93. https://doi.org/10.1530/ERP-20-0026.
15. Lancellotti P, Moura L, Pierard LA, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: Mitral and tricuspid regurgitation (native valve disease). Eur J Echocardiogr 2010;11(4):307-32. https://doi.org/10.1093/ejechocard/jeq031.
16. Friedrich MG, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: A JACC white paper. J Am Coll Cardiol 2009;53(17):1475-87. https://doi.org/10.1016/j.jacc.2009.02.007.
17. Moon JC, Messroghli DR, Kellman P, et al. Myocardial T1 mapping and extracellular volume quantification: A Society for Cardiovascular Magnetic Resonance (SCMR) and CMR Working Group of the European Society of Cardiology consensus statement. J Cardiovasc Magn Reson 2013;15(1):92. https://doi.org/10.1186/1532-429X-15-92.
18. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: Expert recommendations. J Am Coll Cardiol 2018;72(24):3158-76. https://doi.org/10.1016/j.jacc.2018.09.072.
19. Kramer CM, Barkhausen J, Flamm SD, et al. Standardized cardiovascular magnetic resonance (CMR) protocols 2013 update. J Cardiovasc Magn Reson 2013;15(1):91. https://doi.org/10.1186/1532-429X-15-91.
20. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105(4):539-42. https://doi.org/10.1161/hc0402.102975.
21. Chesler E, King RA, Edwards JE. The myxomatous mitral valve and sudden death. Circulation 1983;67(3):632-9. https://doi.org/10.1161/01.CIR.67.3.632.
22. Al-Sadawi M, Aslam F, Tao M, et al. Association of late gadolinium enhancement in cardiac magnetic resonance with mortality, ventricular arrhythmias, and heart failure in patients with nonischemic cardiomyopathy: A systematic review and meta-analysis. Heart Rhythm O2 2023;4(4):241-50. https://doi.org/10.1016/j.hroo.2023.01.001.
23. Liu T, Ma X, Liu W, et al. Late gadolinium enhancement amount as an independent risk factor for the incidence of adverse cardiovascular events in patients with stage C or D heart failure. Front Physiol 2016;7:484. https://doi.org/10.3389/fphys.2016.00484.
24. Todiere G, Nugara C, Gentile G, et al. Prognostic role of late gadolinium enhancement in patients with hypertrophic cardiomyopathy and low-to-intermediate sudden cardiac death risk score. Am J Cardiol 2019;124(8):1286-92. https://doi.org/10.1016/j.amjcard.2019.07.023.