Common Phenotype in Patients With Mitral Valve Prolapse Who Experienced Sudden Cardiac Death

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Mitral valve prolapse (MVP) is a prevalent valvular condition with heterogeneous outcomes.[1,2] Excess mortality is associated with moderate-to-severe mitral regurgitation (MR) and reduced left ventricular ejection fraction.[2] Whereas MVP is considered benign in patients without such risk factors,[1,2] some reports have described ventricular arrhythmias and sudden death (SD) in apparently uncomplicated MVP.[3,4] Moreover, MVP was identified in 42% of patients who experienced idiopathic out-of-hospital cardiac arrest.[3]

The aim of this study was to collect exhaustive clinical and laboratory characteristics of patients with MVP who survived SD without any other obvious explanation.

This international study involved 9 tertiary centers, 8 in France and 1 in the United States. From the database of adults implanted with a cardioverter-defibrillator between 1996 and 2014 at each center, we included all the patients after surviving documented ventricular fibrillation with no detectable structural or electric cause other than MVP. We analyzed clinical, ECG, and echocardiographic characteristics collected before SD when available, <3 months and ≥3 months after SD. Patients with a history of heart surgery before SD were excluded. Follow-up data of implanted cardioverter-defibrillator interrogations were collected until the patients were eventually referred for heart surgery. The patients gave informed consent for this observational study for which institutional review board approval was obtained.

Forty-two patients were included (data from 10 of whom were included in a previous report)[3] (Table). We observed a common phenotype characterized by syncope, frequent and repetitive premature ventricular contractions (PVCs) originating from the posterior papillary muscle in patients characterized as having "severe myxomatous MVP disease" (defined by the combination of bileaflet prolapse, myxomatous mitral valve with thickened leaflet, and mitral annular disjunction). The majority of patients had no, mild, or mild-to-moderate MR. Such an echocardiographic pattern was found in 96% of the 25 patients in whom it could be assessed. The PVCs originating from posterior papillary muscle had prolonged QRS duration (167±19 ms) with a low prematurity index (1.4±0.1) based on R-R/QT interval ratio.

Among 32 patients with repeat echocardiograms, MVP characteristics were similar before and after SD, including bileaflet prolapse (28 versus 28, P=0.99), myxomatous leaflets (32 versus 32, P=0.99), and mitral annular disjunction (19 versus 19, P=0.99), with a similar grade of MR within 3 months of SD (median grade, 2 versus 2, P=0.58). Left ventricular ejection fraction was comparable before and at >3 months after SD (63.6±4.0% versus 60.9±6.4%; P=0.98). Similarly, there was no change in the prevalence of PVCs of any origin (P=0.26) and of PVCs from posterior papillary muscle origin (P=0.14).

*Drs Hourdain and Clavel contributed equally and are joint first authors.

Key Words: death, sudden ■ defibrillators, implantable ■ mitral valve insufficiency ■ mitral valve prolapse ■ risk factors

Table. Clinical, Echocardiographic, and ECG Characteristics of Cases

Variables	n
Clinical variables	n=42
Women	28 (67)
Body surface area, m^2	1.9±0.2
Age at MVP diagnosis, years	37±15
Age at SD, years	45±15
Time from MVP diagnosis to SD, months	63 (0–156)
Family history of MVP, patients	6 (14)
Family history of SD, patients	8 (19)
Atrial fibrillation before SD, patients	7 (17)
Symptoms before SD, patients	
Presyncope	40 (95)
Syncope	24 (59)
Chest pain	16 (38)
Palpitations	39 (93)
Dyspnea	1 (2)
Patients on antiarrhythmic drugs before SD	11 (26)
Class I, n / class II, n / class III, n‖*	1/9/5
Mitral valve surgery after SD,¶†, patients	4 (9)
ICD follow-up	n=42
Duration, months	63 (4–120)
VF recurrence, patients	16 (38)
VT recurrence, patients	22 (52)
Appropriate shocks per patient	3 (1–16)
Echocardiographic variables*	
From reports	n=42
Bileaflet MVP, patients	37 (88)
Myxomatous MVP, patients	42 (100)
Left ventricle ejection fraction, %	62±5
Flail leaflet, patients	5 (12)
LVED diameter, mm	55±5
LVES diameter, mm	37±5
Systolic right ventricular pressure, mm Hg	29±5
Mitral regurgitation, patients, n (%)	
None or trivial	8 (19)
Mild or mild-to-moderate	29 (69)
Moderate or severe	5 (12)
Measured data§	n=25
Mitral annular disjunction, patients	25 (100)
Height of mitral prolapse, mm	13±3
Mitral annular diameter, cm	4.3±0.4
Anterior/posterior mitral leaflets	
Length, cm	2.9±0.4/2.4±0.2
Proximal thickness, mm	3.7±0.7/6.2±1.7
Distal thickness, mm	7.7±1.5/7.4±1.5
ECG variables†	n=42
ECG tracings per patient	7.9±6.9
QRS duration, ms	98±13
Corrected QT interval, ms	426±23
Patients with PVCs	42 (100)
Patients with NSVT	15 (36)
ECG tracings with PVCs, %	69
ECG tracings with PVC bigeminy/couplets, %	44/26
PVC characteristics by origin‡	n=39
PVC prevalence, patients	
Posterior papillary muscle	38 (97)
Anterior papillary muscle	28 (72)
Anterior mitral annulus	18 (46)
Posterior mitral annulus	15 (39)
Right/left outflow tract	14 (36)
Proportion among all PVCs per patient, %	
Posterior papillary muscle	55
Anterior papillary muscle	14
Anterior mitral annulus	13
Posterior mitral annulus	11
Right/left outflow tract	7

Values are mean±standard deviation, n (%), or median (interquartile range). ICD indicates implantable cardioverter defibrillator; LVED, left ventricular end-diastolic; LVES, left ventricular end-systolic; MVP, mitral valve prolapse; NSVT, nonsustained ventricular tachycardia; PVC, premature ventricular contraction; SD, sudden death; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Echocardiography recorded at the time of SD for analysis.

†The constancy over time of the phenotype allowed us to pull all available ECG data together as a same set in each patient.

‡Patients for whom PVC morphology was available on 12-lead ECG to assess their origin.

§Patients with available echocardiogram records for additional measurements.

‖Some patients received antiarrhythmic drug combinations.

¶One patient missing data.

Over the mean follow-up of 110.7±105.6 months, 5 patients received ≥1 shock, with a median of 3 ange, 1–16) appropriate shocks per patient. Nine atients received inappropriate shocks; 1 had an atrial brillation history. The patients who received appropri-te shocks showed no differences over the period from D to last follow-up in terms of left ventricle ejection action (52±15% versus 58±7%, *P*=0.68), left ventri-e end-diastolic diameter (61±5 mm versus 59±4 mm, =0.89), left ventricle end-systolic diameter (42±4 mm ersus 40±2 mm, *P*=0.59), and MR grade (2 [2–2] versus [2–4], *P*=0.09).

We report the largest international case series of esuscitated patients with SD in whom MVP was the nly detectable cause. Sudden death cannot be ex-lained by a natural history of severe MR because it ccurs in patients with a normal left ventricular ejec-ion fraction and, for most, no, mild, or mild-to-mod-erate MR.[2] We went beyond the often mentioned and separately described thickened bileaflet prolapse,[3,4]

inadequate to identify patients at risk of SD because of its high prevalence in MVP. We reported a "severe myxomatous mitral prolapse disease" characterized by the above-mentioned features combined with mitral annular disjunction, an abnormality recently associated with left ventricular late enhancement in the papillary muscles and inferobasal wall on cardiovascular magnetic resonance imaging.[4]

Our patients demonstrated frequent and polymorphic ventricular arrhythmias originating primarily from the posterior papillary muscle with typical prolonged duration,[5] known to represent ventricular arrhythmia triggers. Extrasystole prematurity, involved in idiopathic ventricular fibrillation, was unimpressive. In contrast to a previous publication,[3] right/left outflow-tract PVCs, known to be mostly benign, were not predominant in our patients. Long-term follow-up demonstrated life-threatening arrhythmia recurrences, showing that cardiac arrest is not an isolated event. The stability over time of the entire phenotype confirmed that these findings are not consequent to SD.

Our conclusions are drawn from a small sample, but, to our knowledge, this is the largest reported cohort of patients who have MVP with SD and are still alive. At the inclusion, no data were published on the relationship between arrhythmic MVP and myocardial scar on cardiovascular magnetic resonance, explaining that it is absent or inhomogeneous in many of our cases, precluding discussion of this important consideration.

Our findings could guide further research to assess a multiparametric approach of SD risk stratification in patients with MVP, allowing identification of higher-risk patients and reassurance for those with a low-risk MVP phenotype.

ARTICLE INFORMATION

Data sharing: The data that support the findings of this study are available from the corresponding author on reasonable request.

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Disclosures

None.

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