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Pronounced Mitral Annular Disjunction Is Associated with Increased Ventricular Arrhythmia Burden After Mitral Valve Surgery

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Abstract

Mitral annular disjunction (MAD) has been associated with ventricular arrhythmias in mitral valve prolapse, while postoperative ventricular arrhythmia burden remains incompletely characterized. We aimed to assess objective ventricular arrhythmia burden after mitral valve surgery in patients with and without pronounced MAD (pMAD). In this retrospective single-center cohort with cross-sectional postoperative rhythm assessment, patients undergoing mitral valve surgery for Barlow's disease between 2014 and 2023 were stratified by intraoperative transesophageal echocardiography into pMAD (≥8 mm) and non-pMAD (<8 mm). All patients were invited to structured postoperative follow-up, including 24-h Holter monitoring at variable time points after surgery. Valid recordings were available in 126 of 246 patients (51.2%; 66 pMAD, 60 non-pMAD). Patients with pMAD had a significantly higher ventricular ectopic burden than those without pMAD (median 20.1 vs. 5.5 VES/h; $p = 0.005$). Non-sustained ventricular tachycardia was documented exclusively in the pMAD group (15.2% vs. 0%; $p = 0.001$). After multivariable adjustment, pMAD remained associated with high ventricular ectopic burden (OR 3.38, 95% CI 1.32–8.64; $p = 0.011$). These findings identify pMAD as a marker of increased postoperative ventricular arrhythmia burden after mitral valve surgery for Barlow's disease.

Keywords: mitral valve surgery; mitral annular disjunction; Barlow's disease; ventricular arrhythmias; ventricular ectopy; non-sustained ventricular tachycardia; Holter monitoring

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1. Introduction

Mitral annular disjunction (MAD) is a structural separation between the mitral annulus and left ventricular myocardium frequently observed in myxomatous mitral valve disease and mitral valve prolapse [1–5]. MAD has been associated with ventricular arrhythmias and sudden cardiac death [6–10], potentially reflecting chronic mechanical stress, myocardial fibrosis, and electrical heterogeneity [11–16].

While previous studies have primarily focused on untreated MVP populations, postoperative ventricular arrhythmia burden in patients with MAD remains incompletely characterized [6,8,17,18]. Recent surgical data suggest an increased long-term risk of ventricular

arrhythmias after mitral valve surgery, but quantitative Holter-based comparisons of pMAD and non-pMAD patients within a homogeneous Barlow cohort remain limited [19].

In a previous study from our group, pronounced MAD (≥8 mm) was associated with increased postoperative palpitations despite successful mitral valve surgery [20]. However, objective postoperative rhythm correlates were not systematically assessed.

The present study therefore aimed to evaluate postoperative ventricular arrhythmia burden using structured Holter monitoring in patients with and without pronounced MAD following mitral valve surgery for Barlow's disease.

2. Materials and Methods

2.1. Study Design and Population

This retrospective single-center observational cohort study included adult patients undergoing mitral valve surgery for Barlow's disease between 2014 and 2023. Mitral annular disjunction was retrospectively assessed by a single observer using archived intraoperative transoesophageal echocardiographic recordings. MAD measurements were consistently performed at end-systole in a single predefined mid-oesophageal intercommissural TEE view for all patients. No additional imaging planes were used to identify or select a maximum MAD distance. All 246 intraoperative TEE recordings were individually reviewed by a single observer and provided sufficient image quality for reliable identification of the anatomical landmarks required for MAD measurement. No patients were excluded because of inadequate TEE image quality. A representative intraoperative TEE image illustrating the standardized end-systolic measurement of MAD is provided in Supplementary Figure S2. The observer was blinded to subsequent Holter findings at the time of MAD assessment. Mitral annular disjunction was quantified as the longitudinal distance between the atrial wall–mitral leaflet hinge point and the left ventricular myocardial crest at end-systole. A distance of 0 mm indicated no measurable disjunction, whereas any measurable separation greater than 0 mm was recorded as MAD. Pronounced mitral annular disjunction (pMAD) was defined as a distance ≥8 mm. This threshold was selected a priori during study design, before analysis of the postoperative Holter data, informed by previous reports associating larger MAD distances (particularly >8.5 mm) with ventricular arrhythmias and consistent with our earlier investigation of the same surgical cohort. The cutoff was not derived or optimized from the present Holter outcomes and does not represent a validated arrhythmic risk threshold [3,20]. Patients were stratified into pMAD (≥8 mm) and non-pMAD (<8 mm), with the latter group including both lesser degrees of disjunction and no measurable disjunction.

Mitral valve surgery was performed according to the underlying degenerative valve pathology and standard surgical practice. No standardized MAD-specific surgical strategy was applied, and the procedures were not primarily designed to modify or eliminate MAD.

2.2. Ethics and Informed Consent

The study was approved by the Ethics Committee of the Technical University of Munich (protocol 2025-407-S-CB, 19 August 2025). Written informed consent was obtained from all participants in accordance with institutional requirements and the approval of the local ethics committee.

2.3. Follow-Up and Holter Monitoring

All patients in the surgical cohort were invited to participate in a standardized postoperative follow-up examination, irrespective of MAD status. Postoperative 24-h Holter monitoring was routinely performed as part of the standardized study follow-up protocol, irrespective of patient-reported symptoms or clinical suspicion of arrhythmia.

The follow-up protocol included 24-h Holter electrocardiogram monitoring, transthoracic echocardiography, and assessment of health-related quality of life using the SF-36 questionnaire. Holter monitoring was performed at variable time points after surgery using a 12-channel Medilog system (Schiller AG, Baar, Switzerland). Systematic preoperative Holter monitoring was not available for the overall cohort; therefore, the study was designed to assess postoperative arrhythmia burden rather than longitudinal changes in ventricular arrhythmias from before to after surgery. A Holter recording was considered valid if at least 24 h of analyzable recording time were available. Recordings not meeting this predefined duration criterion were excluded from the principal Holter analysis. Patients who attended follow-up but did not undergo Holter monitoring were also excluded from the Holter analysis cohort. Of the overall surgical cohort, patients who did not participate in structured follow-up because they declined participation or could not be reached were classified as not having Holter follow-up available. Rhythm recordings were analyzed according to standardized institutional protocols and manually reviewed in a blinded fashion by experienced personnel of the institutional Holter monitoring unit.

Ventricular ectopic activity was quantified as ventricular extrasystoles per hour (VES/h). Supraventricular ectopic activity was assessed as supraventricular ectopic beats per hour. In addition, the presence and duration of atrial fibrillation were recorded where applicable.

Ventricular tachycardia was defined as three or more consecutive ventricular beats. Episodes were classified as non-sustained ventricular tachycardia (NSVT) if they terminated within 30 s and as sustained ventricular tachycardia if they lasted ≥30 s or required earlier termination because of hemodynamic instability. Heart rate characteristics including bradycardic and tachycardic episodes were documented according to standard Holter definitions.

Given the absence of established postoperative thresholds for clinically relevant ventricular ectopic burden in this population, the upper quartile of VES/h was used as an exploratory distribution-based cutoff to identify patients with increased ventricular ectopic activity.

2.4. Definitions and Outcomes

The primary endpoint of the study was ventricular ectopic burden expressed as VES/h. High ventricular ectopic burden was defined as the upper quartile (Q4) of VES/h, corresponding to a data-derived cutoff of 39.46 VES/h (75 th percentile). Given the skewed distribution of VES burden, exploratory dichotomization using the upper quartile was chosen to facilitate clinically interpretable regression modelling. Secondary endpoints included the occurrence of NSVT, atrial fibrillation prevalence and duration, as well as patient-reported quality of life assessed using the Short Form-36 questionnaire.

2.5. Statistical Analysis

Continuous variables were assessed for normal distribution and are presented as mean ± standard deviation or median with interquartile range, as appropriate. Between-group comparisons were performed using Student's *t*-test or Mann–Whitney U test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, as appropriate.

To assess potential selection bias related to Holter availability, baseline clinical, echocardiographic, and operative characteristics were additionally compared between patients with and without valid postoperative Holter monitoring.

To identify independent predictors of high ventricular ectopic burden, exploratory multivariable logistic regression analysis was performed. Clinically relevant covariates selected a priori were entered into the model, including age, female sex, preoperative atrial fibrillation, body mass index, and arterial hypertension. Odds ratios (ORs) with corre-

sponding 95% confidence intervals (CIs) were calculated. High VES burden (Q4) served as the dependent variable. Given differences in the timing of postoperative Holter monitoring, a sensitivity analysis was performed by additionally including time from surgery to Holter monitoring as a continuous covariate in the multivariable logistic regression model. In an additional sensitivity analysis, time from surgery to Holter monitoring and type of mitral valve surgery (repair versus replacement) were included to account for potential confounding related to follow-up timing and operative treatment. To assess the robustness of the findings independent of the exploratory Q4 cutoff, VES/h was additionally analyzed as a continuous outcome. Because of its skewed distribution, VES/h was natural log-transformed as ln(VES/h + 1) and analyzed using multivariable linear regression including the same prespecified covariates, time from surgery to Holter monitoring, and type of mitral valve surgery. An exploratory sensitivity analysis additionally incorporated contemporaneous follow-up echocardiographic parameters (LVEF, LVEDD, and residual mitral regurgitation ≥ grade II) into a linear regression model adjusted for pMAD status, follow-up duration, and surgical treatment type. As an exploratory analysis of potential effect modification by follow-up timing, ventricular ectopic burden was compared between pMAD and non-pMAD patients within postoperative follow-up intervals of ≤36 and >36 months. In addition, an interaction between pMAD status and time from surgery to Holter monitoring was assessed using linear regression with ln(VES/h + 1) as the dependent variable. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Study Population

A total of 246 patients undergoing mitral valve surgery for Barlow's disease between 2014 and 2023 were included in the overall surgical cohort. Based on intraoperative transoesophageal echocardiography, 103 patients (41.9%) were classified as having pronounced mitral annular disjunction (pMAD ≥ 8 mm), while 143 patients (58.1%) were classified as non-pMAD (<8 mm). Within the non-pMAD group, 13 patients (9.1%) had no measurable disjunction (0 mm), whereas 130 patients (90.9%) had a measurable MAD distance >0 mm and <8 mm.

Of the overall cohort, 147 patients (59.8%) participated in structured postoperative follow-up. Follow-up participation was higher among patients with pMAD than among those without pMAD (70/103 [68.0%] vs. 77/143 [53.8%], $p = 0.026$) Among the 147 follow-up participants, 141 underwent Holter monitoring, whereas six did not undergo Holter monitoring (two pMAD and four non-pMAD). Of the 141 recordings, 15 did not meet the predefined recording-duration criterion (two pMAD and 13 non-pMAD), leaving 126 valid Holter recordings (51.2% of the overall surgical cohort), including 66 patients with pMAD and 60 without pMAD. Among follow-up participants, valid Holter recordings were more frequently available in patients with pMAD than in those without pMAD (66/70 [94.3%] vs. 60/77 [77.9%], $p = 0.005$). In contrast, the proportion of patients undergoing Holter monitoring among follow-up participants did not differ significantly between groups (68/70 [97.1%] vs. 73/77 [94.8%], Fisher's exact $p = 0.683$). Of the 99 patients who did not participate in structured follow-up, 69 declined participation and 30 could not be reached. Median time from surgery to valid Holter monitoring was 34.5 months (IQR 25.0–55.0; range 9–117 months) (Figure 1). The distribution of time from surgery to postoperative Holter monitoring according to pMAD status is illustrated in Supplementary Figure S1.

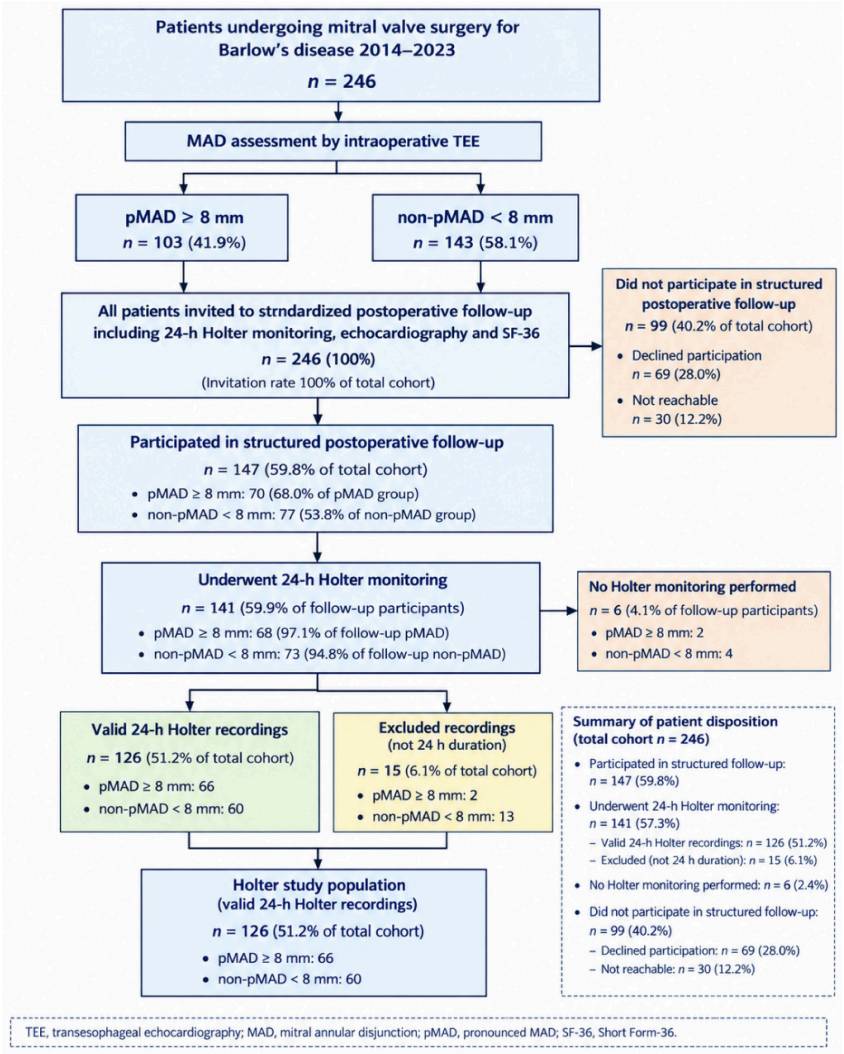


Figure 1. Study flow diagram. Flowchart illustrating patient selection from the overall surgical cohort to the final Holter analysis. Of 246 eligible patients, 147 participated in structured postoperative follow-up, of whom 141 underwent Holter monitoring. Fifteen recordings were excluded because they did not meet the predefined minimum recording duration of 24 h, leaving 126 patients with valid Holter recordings (66 with pMAD and 60 without pMAD). Among the 99 patients who did not participate in structured follow-up, 69 declined participation and 30 could not be reached. MAD, mitral annular disjunction; pMAD, pronounced mitral annular disjunction.

Time from surgery to Holter monitoring differed between groups and was shorter in patients with pMAD than in those without pMAD (median 29.5 [IQR 16.8–49.3] vs. 43.5 [29.0–62.0] months; $p < 0.001$).

Baseline clinical, echocardiographic, and operative characteristics of patients with and without valid Holter monitoring are presented in Supplementary Table S2. pMAD was more frequent among patients with valid Holter monitoring (52.4% vs. 30.8%, $p < 0.001$), and aortic cross-clamp time was shorter (86.3 ± 33.2 vs. 94.8 ± 32.3 min, $p = 0.040$). No other significant differences were observed.

3.2. Baseline Characteristics

Baseline characteristics of the overall surgical cohort ($n = 246$) and the Holter study population ($n = 126$) are presented in Supplementary Table S1 and Table 1, respectively. Patients with pMAD were younger (54.4 ± 11.0 vs. 58.5 ± 11.6 years, $p = 0.042$) and had a

lower body mass index (23.2 ± 2.9 vs. 24.6 ± 3.4 kg/m^2, p =0.018). Other demographic and preoperative clinical characteristics were comparable between groups.

Operative characteristics were largely comparable between groups, except for a higher rate of mitral valve repair in patients with pMAD (93.9% vs. 81.7%, p = 0.034) (Table 1).

Table 1. Baseline characteristics of patients with valid 24-h Holter monitoring.

	All Patients (n = 126)	pMAD (n = 66)	Non-pMAD (n = 60)	p-Value
Demographic characteristics				
Female sex, n (%)	42 (33.3)	19 (28.8)	23 (38.3)	0.282
Age at surgery (years)	56 ± 11.4	54.4 ± 11.0	58.5 ± 11.6	0.042
BMI (kg/m^2)	23.9 ± 3.2	23.2 ± 2.9	24.6 ± 3.4	0.018
Preoperative clinical characteristics				
Arterial hypertension, n (%)	54 (42.9)	25 (37.9)	29 (48.3)	0.236
Hyperlipidemia, n (%)	42 (33.3)	23 (34.8)	19 (31.7)	0.705
Diabetes mellitus, n (%)	3 (2.4)	1 (1.5)	2 (3.3)	0.605
Coronary artery disease, n (%)	8 (6.3)	4 (6.1)	4 (6.7)	1.000
Atrial fibrillation, n (%)	28 (22.2)	16 (24.2)	12 (20.0)	0.567
NYHA class III-IV, n (%)	36 (28.6)	16 (24.2)	20 (33.3)	0.259
Operative characteristics				
Mitral valve repair, n (%)	111 (88.1)	62 (93.9)	49 (81.7)	0.034
Concomitant MAZE, n (%)	10 (7.9)	5 (7.6)	5 (8.3)	1.000
Concomitant tricuspid valve surgery, n (%)	21 (16.7)	9 (13.6)	12 (20.0)	0.338
Concomitant aortic surgery, n (%)	6 (4.8)	3 (4.5)	3 (5.0)	0.905
Concomitant CABG, n (%)	4 (3.2)	2 (3.0)	2 (3.3)	0.923
Cross-clamp time (min)	85.6 ± 32.8	87.4 ± 32.3	83.7 ±33.6	0.532
CPB time (min)	132.2 ± 47.6	134.3 ± 42.3	129.8 ± 53.1	0.597

Values are presented as mean ± standard deviation or n (%), as appropriate. Continuous variables were compared using Student's t-test and categorical variables using the χ^2 test or Fisher's exact test, as appropriate. CAD = coronary artery disease; CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; MAZE = surgical ablation procedure for atrial fibrillation; NYHA = New York Heart Association; pMAD = pronounced mitral annular disjunction.

3.3. Holter-Derived Ventricular Arrhythmia Burden

Holter-derived ventricular arrhythmia burden is summarized in Table 2. Patients with pMAD exhibited a significantly higher burden of ventricular ectopy than those without pMAD (Figure 2).

Table 2. Holter-derived postoperative rhythm characteristics.

	All Patients (n = 126)	pMAD (n = 66)	Non-pMAD (n = 60)	p-Value
VES per hour, median (IQR)	9.0 (1.4–43.5)	20.1 (3.4–59.7)	5.47 (0.7–14.3)	0.005
High VES burden (Q4), n (%)	32 (25.4)	22 (33.3)	10 (16.7)	0.032
Non-sustained ventricular tachycardia (NSVT), n (%)	10 (7.9)	10 (15.2)	0 (0)	0.001
Atrial fibrillation at Holter follow-up, n (%)	6 (4.8)	4 (6.1)	2 (3.3)	0.473

Values are presented as median (interquartile range) or n (%). Continuous variables were compared using the Mann–Whitney U test and categorical variables using the χ^2 test or Fisher's exact test, as appropriate. High ventricular ectopic burden was defined as the upper quartile (Q4) of ventricular extrasystoles per hour. Ventricular tachycardia was defined as ≥3 consecutive ventricular beats; all detected episodes were non-sustained (<30 s duration).

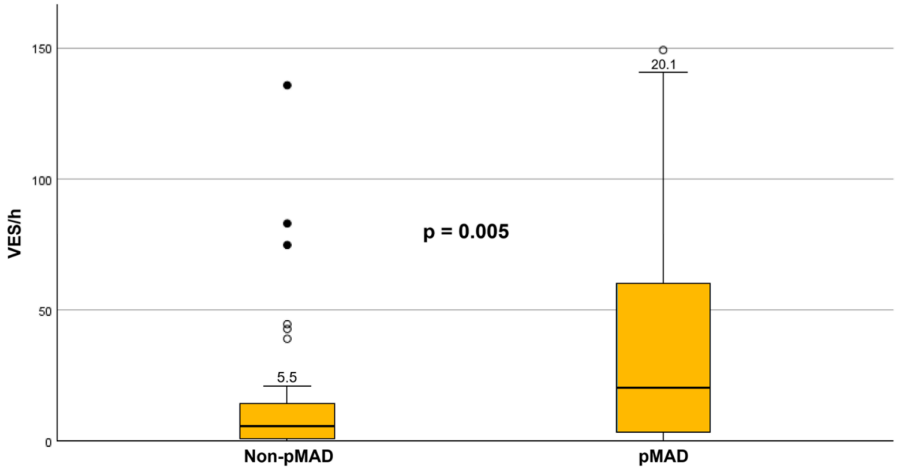


Figure 2. Postoperative ventricular ectopic burden according to MAD status. Comparison of ventricular extrasystoles per hour (VES/h) recorded during postoperative 24-h Holter monitoring in patients with pronounced mitral annular disjunction (pMAD; $n = 66$) and without pMAD ($n = 60$). Patients with pMAD exhibited a significantly higher ventricular ectopic burden than those without pMAD (median 20.1 vs. 5.5 VES/h; $p = 0.005$). MAD, mitral annular disjunction; VES, ventricular extrasystoles.

Median VES per hour was markedly increased in the pMAD group (20.1 [3.4–59.7]) compared with the non-pMAD group (5.47 [0.7–14.3], $p = 0.005$). Consistently, a high VES burden, defined as the upper quartile of VES per hour, was more frequently observed in patients with pMAD (33.3% vs. 16.7%, $p = 0.032$). Non-sustained ventricular tachycardia (NSVT) was documented exclusively in the pMAD group (15.2% vs. 0%; $p = 0.001$) (Figure 3).

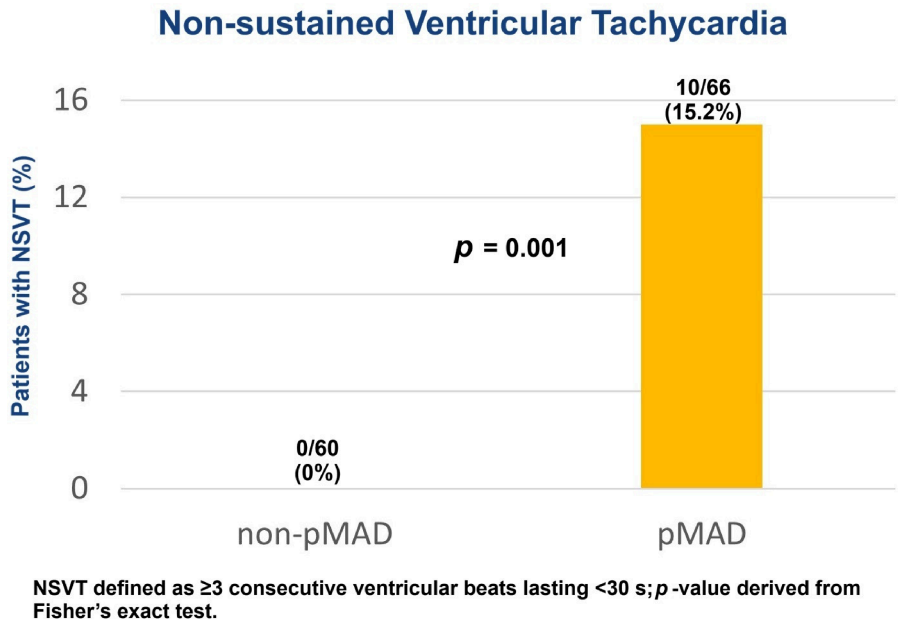


Figure 3. Prevalence of non-sustained ventricular tachycardia according to MAD status. Bar chart comparing the proportion of patients with non-sustained ventricular tachycardia (NSVT) detected during postoperative 24-h Holter monitoring in patients with pronounced mitral annular disjunction (pMAD; $n = 66$) and without pMAD ($n = 60$). NSVT was documented in 10 patients with pMAD (15.2%) and in none of the patients without pMAD (0%; $p = 0.001$). No sustained ventricular tachycardia was recorded. MAD, mitral annular disjunction; NSVT, non-sustained ventricular tachycardia.

No sustained ventricular tachycardia was documented during postoperative Holter monitoring. Postoperative rhythm-related therapies, including beta-blocker therapy, electrical cardioversion, catheter ablation, pacemaker/ICD implantation, and oral anticoagulation, were comparable between groups (Table 3). Likewise, atrial fibrillation prevalence at Holter follow-up did not differ significantly (Table 2).

Table 3. Follow-up rhythm-related therapies/interventions.

	All Patients (n = 126)	pMAD (n = 66)	Non-pMAD (n = 60)	p-Value
Beta-blocker therapy, n (%)	48 (38.1)	24 (36.4)	24 (40.0)	0.508
Electrical cardioversion after surgery, n (%)	14 (11.1)	8 (12.1)	6 (10.0)	0.506
Catheter ablation after surgery, n (%)	20 (15.9)	13 (19.7)	7 (11.7)	0.313
Pacemaker/ICD implantation after surgery, n (%)	9 (7.1)	3 (4.5)	6 (10.0)	0.275
Oral anticoagulation at follow-up, n (%)	26 (20.6)	13 (19.7)	13 (21.7)	0.546

Values are presented as n (%). Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate.

3.4. Multivariable Analysis

Results of the multivariable logistic regression analysis for high VES burden (Q4) are shown in Table 4. After adjustment for age, female sex, body mass index, arterial hypertension, and atrial fibrillation, pMAD remained associated with a high VES burden (odds ratio 3.38, 95% confidence interval 1.32–8.64, $p = 0.011$). No other variables were significantly associated with high VES burden in the multivariable model, although body mass index showed a borderline association (OR 1.15, 95% CI 1.00–1.33, $p = 0.055$). In a sensitivity analysis additionally adjusting for time from surgery to Holter monitoring, the association between pMAD and high VES burden remained significant (OR 3.61, 95% CI 1.37–9.49, $p = 0.009$), whereas time from surgery to Holter monitoring was not associated with high VES burden (OR 1.006 per month, 95% CI 0.987–1.024, $p = 0.552$) (Supplementary Table S3). In an additional sensitivity analysis accounting for both time from surgery to Holter monitoring and type of mitral valve surgery, pMAD remained significantly associated with high VES burden (OR 2.75, 95% CI 1.11–6.83, $p = 0.029$), whereas neither follow-up time (OR 1.008 per month, 95% CI 0.990–1.026, $p = 0.396$) nor mitral valve repair (OR 1.03, 95% CI 0.26–4.12, $p = 0.967$) was associated with high VES burden (Supplementary Table S3). Finally, when VES/h was analyzed as a continuous log-transformed outcome, pMAD remained independently associated with greater ventricular ectopic burden after adjustment for the prespecified covariates, time from surgery to Holter monitoring, and type of mitral valve surgery (B = 1.096, 95% CI 0.480–1.712, $p < 0.001$) (Supplementary Table S3). Exponentiation of the regression coefficient indicated an approximately threefold higher adjusted geometric mean of (VES/h + 1) in patients with pMAD compared with those without pMAD ($e^B = 2.99$, 95% CI 1.62–5.54). Contemporaneous follow-up echocardiography was available for all 126 patients with valid Holter recordings. In an exploratory sensitivity analysis additionally accounting for LVEF, LVEDD, and residual mitral regurgitation ≥ grade II, as well as follow-up duration and surgical treatment type, pMAD remained associated with ln(VES/h + 1) (B = 0.943, 95% CI 0.343–1.544; $p = 0.002$) (Supplementary Table S4).

In an additional exploratory analysis, no statistically significant interaction was observed between pMAD status and time from surgery to Holter monitoring when follow-up duration was modelled as a continuous variable ($p = 0.121$).

In an exploratory analysis stratified by time from surgery to Holter monitoring, ventricular ectopic burden did not differ significantly between patients with and without

pMAD within 36 months after surgery (pMAD: $n = 40$; non-pMAD: $n = 26$; Mann–Whitney U = 449, $p = 0.351$). Beyond 36 months, ventricular ectopic burden was significantly higher in patients with pMAD (pMAD: $n = 26$; non-pMAD: $n = 34$; Mann–Whitney U = 217, $p < 0.001$).

Table 4. Multivariable logistic regression analysis for high VES burden (Q4).

	Odds Ratio (95% CI)	*p*-Value
pMAD	3.38 (1.32–8.64)	0.011
Age at surgery (per year)	1.01 (0.97–1.06)	0.505
Female sex	1.91 (0.74–4.93)	0.183
Atrial fibrillation	0.91 (0.29–2.90)	0.879
BMI (kg/m^2)	1.15 (1.00–1.33)	0.055
Arterial hypertension	0.47 (0.17–1.29)	0.142

3.5. Association Between MAD Distance and Ventricular Ectopic Burden

In univariable linear regression, MAD distance showed a positive but non-significant association with ln(VES/h + 1) (B = 0.068 per mm, 95% CI −0.013 to 0.149; $p = 0.100$). After adjustment for time from surgery to Holter monitoring and mitral valve repair versus replacement, the association remained positive but did not reach conventional statistical significance (B = 0.085 per mm, 95% CI −0.001 to 0.170; $p = 0.051$). In an exploratory sensitivity analysis using 2000 bootstrap resamples, the bias-corrected and accelerated 95% confidence interval was 0.006 to 0.170. Figure 4 illustrates the unadjusted relationship between MAD distance and postoperative ventricular ectopic burden.

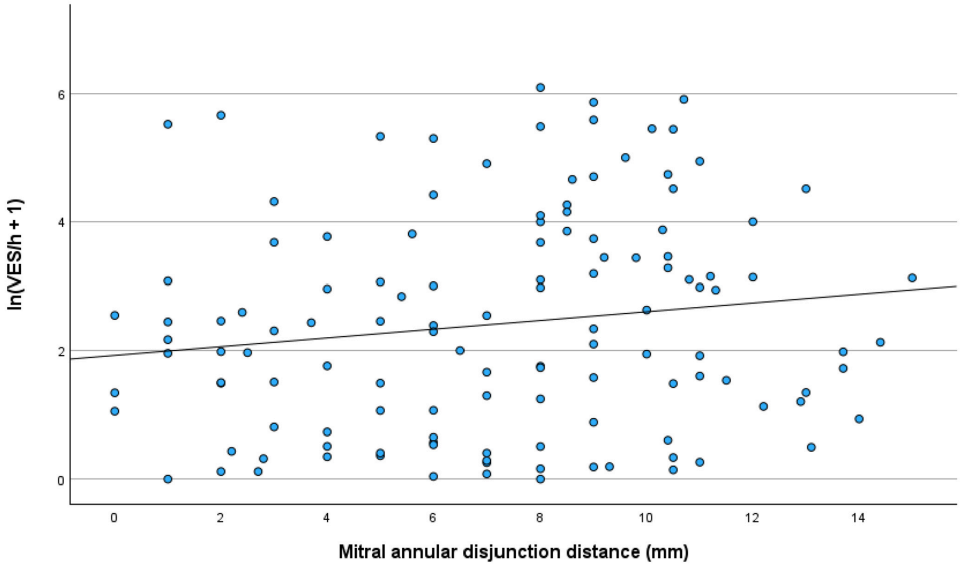


Figure 4. Association between MAD distance and ventricular ectopic burden. Scatter plot illustrating the relationship between mitral annular disjunction (MAD) distance and log-transformed ventricular extrasystoles per hour [ln(VES/h + 1)]. The solid line represents the unadjusted linear regression fit. The association was positive but did not reach statistical significance (B = 0.068 per mm, 95% CI −0.013 to 0.149; $p = 0.100$).

4. Discussion

Pronounced MAD was associated with increased postoperative ventricular arrhythmia burden following mitral valve surgery for Barlow's disease. Ventricular ectopic burden was higher in patients with pMAD, and non-sustained ventricular tachycardia was documented exclusively in this group. The association remained robust in sensitivity analyses accounting

for follow-up timing and type of mitral valve surgery and when VES/h was analyzed as a continuous outcome [6,7,17,19].

Mitral annular disjunction has increasingly been recognized as a structural marker associated with ventricular arrhythmias and sudden cardiac death [6–8]. While previous studies mainly focused on untreated MVP populations, postoperative rhythm characteristics remain insufficiently characterized [8,17]. Our findings extend the current evidence by providing objective postoperative Holter data, addressing a knowledge gap that has recently been highlighted in a comprehensive state-of-the-art review on MAD [18]. Mitral valve surgery modifies annular geometry and corrects mitral regurgitation, raising the question of how these changes relate to subsequent ventricular arrhythmias [5,21]. Recent surgical series have reported ventricular arrhythmias after mitral valve intervention. Our findings complement these studies by providing structured quantitative Holter-based assessment of postoperative ventricular ectopic burden and a direct comparison between patients with and without pMAD within a homogeneous surgical cohort of Barlow's disease. However, in the absence of systematic preoperative Holter monitoring, the present study cannot determine whether ventricular arrhythmia burden increased, decreased, or remained unchanged after surgery [19,22,23].

The ≥8 mm cutoff was informed by previous literature associating larger MAD distances (>8.5 mm) with ventricular arrhythmias and was consistent with our earlier investigation of the same surgical cohort; however, it does not represent a validated threshold for postoperative arrhythmic risk [3,17,20]. As the non-pMAD group also included patients with lesser degrees of disjunction, our findings should not be interpreted as establishing a discrete risk threshold.

When MAD distance was analyzed as a continuous variable, the adjusted linear regression demonstrated a positive association with postoperative ventricular ectopic burden that narrowly missed conventional statistical significance. Although the exploratory bootstrap confidence interval excluded zero, these findings do not establish a linear dose–response relationship. The continuous analysis should therefore be interpreted cautiously, particularly in view of the retrospective study design and potential residual confounding. Greater MAD extent has previously been associated with myocardial fibrosis and ventricular arrhythmias [6,8,11,13]. Chronic mechanical stress and inferolateral fibrosis may provide a mechanistic framework for the increased postoperative ventricular ectopic burden observed in patients with pMAD [11,12,14,19].

From a clinical perspective, the present findings do not support routine intensified rhythm surveillance solely on the basis of pMAD. Nevertheless, the observation that non-sustained ventricular tachycardia occurred exclusively in patients with pMAD warrants further investigation in larger prospective cohorts, as the limited number of events does not permit conclusions regarding the risk of sustained ventricular arrhythmias or sudden cardiac death.

Potential arrhythmogenic mechanisms include abnormal mechanical traction on the papillary muscles and inferobasal left ventricular myocardium, myocardial fibrosis, and the resulting electrical heterogeneity, which may provide a substrate for ventricular tachyarrhythmias [7,11,17]. Cases of ventricular fibrillation and resuscitated sudden cardiac arrest associated with mitral annular disjunction have been reported, illustrating the potential severity of the arrhythmic phenotype [24]. Importantly, all ventricular tachycardia episodes detected in our cohort were non-sustained, and our study cannot establish the risk of sustained ventricular tachycardia, ventricular fibrillation, or sudden cardiac death.

Isolated pMAD does not constitute an indication for implantable cardioverter-defibrillator (ICD) implantation. In survivors of sudden cardiac arrest due to ventricular fibrillation or hemodynamically unstable ventricular tachycardia, however, ICD implan-

tation is recommended for secondary prevention when reversible causes have been excluded and guideline criteria are met [17,25]. The potential psychological burden and impact on quality of life associated with cardiac implantable electronic devices should also be considered [26].

In patients with pMAD and persistent symptoms, complex ventricular ectopy, or additional established arrhythmic risk markers, prolonged rhythm monitoring and cardiac magnetic resonance imaging may be considered for further risk stratification [17,27]. Genetic evaluation may be appropriate in selected patients with unexplained malignant ventricular arrhythmias, suspected inherited arrhythmia syndromes, or a suggestive family history, but isolated pMAD does not warrant routine genetic testing [17,25]. In cases of unexplained sudden cardiac death, postmortem genetic testing may help identify underlying inherited cardiac conditions and guide screening of surviving relatives [28].

The present findings support further prospective evaluation of pMAD as a potential marker of postoperative ventricular ectopic burden. However, whether pMAD-guided rhythm surveillance or individualized risk stratification improves clinical outcomes remains unknown.

The present findings also provide a potential mechanistic explanation for previously observed postoperative palpitations in patients with pMAD [20]. The alignment between previously observed subjective symptom burden and the objectively increased ventricular ectopic burden identified in the present study supports the clinical relevance of postoperative rhythm assessment in this population [20].

Limitations

The single-center design and moderate sample size may limit generalizability. Valid 24-h Holter recordings were available for only 126 of 246 patients (51.2%). Although all patients were invited to the same standardized postoperative follow-up protocol, patients with pMAD were more likely to attend follow-up and to have valid Holter recordings. Among patients attending follow-up, the difference in valid Holter availability was predominantly attributable to recordings not meeting the predefined duration criterion rather than differences in whether Holter monitoring was performed. These findings indicate potential selection bias related to differential follow-up participation and recording validity. Although participation may have been influenced by symptoms or other unmeasured characteristics, the reasons for participation were not systematically recorded. As ventricular ectopic burden was unavailable for patients without valid Holter recordings, the direction and magnitude of the resulting selection bias cannot be reliably determined. If patients with pMAD and a higher arrhythmic or symptom burden were more likely to participate in follow-up or provide valid Holter recordings, the observed association may have been overestimated. Conversely, the absence of ventricular arrhythmia data from patients without valid recordings prevents a reliable assessment of the direction or magnitude of this potential bias. Therefore, the findings may not be fully generalizable to the entire surgical cohort. The definition of high ventricular ectopic burden was based on the upper quartile of the observed VES/h distribution and should therefore be interpreted as an exploratory, cohort-specific threshold rather than an established clinical risk cutoff.

Holter monitoring was performed at variable postoperative time points, with a shorter interval from surgery to Holter monitoring in patients with pMAD. However, the association between pMAD and ventricular ectopic burden remained significant in sensitivity analyses accounting for time from surgery to Holter monitoring and type of mitral valve surgery, as well as when VES/h was analyzed as a continuous log-transformed outcome. Nevertheless, residual temporal and treatment-related confounding cannot be excluded. The reasons underlying the different intervals between surgery and Holter monitoring could

not be reliably determined retrospectively. Therefore, differences in follow-up participation, survivorship, and unmeasured postoperative events may have contributed to the observed timing imbalance.

Exploratory analyses stratified by follow-up duration showed a significant difference in ventricular ectopic burden between pMAD and non-pMAD patients beyond 36 months, but not within the first 36 months after surgery. However, the formal interaction between pMAD status and follow-up duration was not statistically significant ($p = 0.121$). Therefore, these findings should not be interpreted as evidence of a time-dependent increase in ventricular ectopic burden. Given the variable timing and cross-sectional nature of postoperative Holter monitoring, residual temporal confounding cannot be excluded.

Furthermore, systematic preoperative Holter monitoring was not available, precluding longitudinal assessment of changes in ventricular arrhythmia burden from before to after surgery. Consequently, the present study cannot determine the effect of mitral valve surgery on ventricular arrhythmia burden and should be interpreted as a postoperative cross-sectional rhythm assessment within a retrospectively defined surgical cohort. Although additional adjustment for mitral valve repair versus replacement was performed, residual confounding related to more detailed procedural characteristics, including annuloplasty ring type and size, cannot be excluded. Arrhythmia assessment was based on a single postoperative 24-h Holter recording per patient, routinely obtained as part of the standardized study follow-up protocol irrespective of patient-reported symptoms or clinical suspicion of arrhythmia. This limited sampling window may underestimate intermittent ventricular arrhythmias. Continuous inpatient telemetry recordings, prior ambulatory rhythm monitoring, and device-derived arrhythmia data were not systematically available for analysis. Although information on pacemaker and ICD implantation was available, these procedural events do not permit reliable quantification of arrhythmia burden.

Furthermore, the study was not powered to assess hard clinical endpoints such as sudden cardiac death, appropriate ICD therapies, or long-term cardiovascular outcomes. Although non-sustained ventricular tachycardia was documented exclusively in patients with pMAD, the small number of events precluded meaningful adjusted analyses. Detailed episode characteristics, including run length, maximum heart rate, and morphology, as well as associated symptoms and subsequent clinical management, were not systematically documented and could therefore not be reliably evaluated. Furthermore, arrhythmia-related hospitalizations, syncope, appropriate ICD therapies, and the indications and timing of rhythm-related interventions were not systematically captured. Consequently, the clinical significance and prognostic implications of the observed NSVT episodes remain uncertain.

Finally, MAD was retrospectively assessed from archived intraoperative transoesophageal echocardiographic recordings by a single observer, and interobserver and intraobserver reproducibility were not evaluated. Although MAD assessment was performed blinded to subsequent Holter findings, measurement variability and the absence of a universally accepted gold standard for MAD assessment may have affected classification accuracy. MAD was not systematically assessed using preoperative transthoracic echocardiography, cardiac magnetic resonance imaging, or computed tomography. No cardiac magnetic resonance data on myocardial fibrosis or late gadolinium enhancement were available for analysis. Therefore, the relationship between myocardial fibrosis, pMAD, and postoperative ventricular ectopic burden could not be investigated in this cohort.

Although contemporaneous follow-up echocardiographic data were available for the Holter cohort, serial assessment of left ventricular remodeling and systematic postoperative evaluation of residual or recurrent MAD were not available. The additional echocardiography-adjusted analysis was exploratory, and the possibility that postoperative imaging parameters represent mediators rather than confounders should be considered.

Although the association between pMAD and high ventricular ectopic burden remained significant after adjustment for mitral valve repair versus replacement, this binary distinction does not adequately capture the heterogeneity of surgical techniques. Detailed procedural characteristics, including leaflet resection, neochordal implantation, annuloplasty ring type and size, and prosthesis type, were not comprehensively evaluated in relation to postoperative ventricular arrhythmia burden. These procedural factors, as well as the degree of postoperative anatomical correction of MAD, may influence ventricular mechanics and arrhythmogenic substrate. Therefore, residual procedural confounding cannot be excluded, and the observed association should not be interpreted as evidence that pMAD itself is the causal determinant of postoperative ventricular ectopic burden.

5. Conclusions

Among patients assessed during postoperative follow-up after mitral valve surgery for Barlow's disease, pronounced mitral annular disjunction was associated with increased ventricular ectopic burden. Non-sustained ventricular tachycardia was observed exclusively in patients with pMAD, although the small number of events limits conclusions regarding clinically significant ventricular arrhythmias. These observational findings support further prospective investigation of pMAD as a potential marker of postoperative ventricular arrhythmia burden.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcdd13110545/s1, Table S1: Overall Baseline Characteristics; Table S2: Comparison of baseline clinical, echocardiographic, and operative characteristics between patients with and without valid 24-h Holter monitoring; Table S3: Sensitivity analyses of the association between pronounced mitral annular disjunction and ventricular ectopic burden; Table S4: Exploratory follow-up echocardiographic comparisons and echocardiography-adjusted sensitivity analysis of postoperative ventricular ectopic burden; Figure S1: Distribution of time from surgery to postoperative Holter monitoring according to pMAD status; Figure S2: Representative intraoperative transoesophageal echocardiographic image illustrating the standardized end-systolic measurement of mitral annular disjunction.

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Data Availability Statement: The data presented in this study are not publicly available due to privacy and ethical restrictions. Data may be made available from the corresponding author upon reasonable request and subject to approval by the institutional review board.

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Abbreviations

The following abbreviations are used in this manuscript:

AF	Atrial fibrillation
BMI	Body mass index
CABG	Coronary artery bypass grafting
CI	Confidence interval
CPB	Cardiopulmonary bypass
ICD	Implantable cardioverter-defibrillator
IQR	Interquartile range
LVEDD	Left ventricular end-diastolic diameter
LVEF	Left ventricular ejection fraction
MAD	Mitral annular disjunction
MAZE	Surgical ablation procedure for atrial fibrillation
MVP	Mitral valve prolapse
NSVT	Non-sustained ventricular tachycardia
NYHA	New York Heart Association
OR	Odds ratio
pMAD	Pronounced mitral annular disjunction
TEE	Transoesophageal echocardiography
VES	Ventricular extrasystoles

References

1. Hutchins, G.M.; Moore, G.W.; Skoog, D.K. The association of floppy mitral valve with disjunction of the mitral annulus fibrosus. *N. Engl. J. Med.* **1986**, *314*, 535–540. [CrossRef] [PubMed]
2. Angelini, A.; Ho, S.Y.; Anderson, R.H.; Becker, A.E.; Davies, M.J. Disjunction of the mitral annulus in floppy mitral valve. *N. Engl. J. Med.* **1988**, *318*, 188–189. [CrossRef] [PubMed]
3. Carmo, P.; Andrade, M.J.; Aguiar, C.; Rodrigues, R.; Gouveia, R.; Silva, J.A. Mitral annular disjunction in myxomatous mitral valve disease: A relevant abnormality recognizable by transthoracic echocardiography. *Cardiovasc. Ultrasound* **2010**, *8*, 53. [CrossRef]
4. Bennett, S.; Tafuro, J.; Duckett, S.; Appaji, A.; Khan, J.N.; Heatlie, G.; Cubukcu, A.; Kwok, C.S. Definition, prevalence, and clinical significance of mitral annular disjunction in different patient cohorts: A systematic review. *Echocardiography* **2022**, *39*, 514–523. [CrossRef] [PubMed]
5. Eriksson, M.J.; Bitkover, C.Y.; Omran, A.S.; David, T.E.; Ivanov, J.; Ali, M.J.; Woo, A.; Siu, S.C.; Rakowski, H. Mitral annular disjunction in advanced myxomatous mitral valve disease: Echocardiographic detection and surgical correction. *J. Am. Soc. Echocardiogr. Off. Publ. Am. Soc. Echocardiogr.* **2005**, *18*, 1014–1022. [CrossRef] [PubMed]
6. Dejgaard, L.A.; Skjølsvik, E.T.; Lie, Ø.H.; Ribe, M.; Stokke, M.K.; Hegbom, F.; Scheirlynck, E.S.; Gjertsen, E.; Andresen, K.; Helle-Valle, T.M.; et al. The Mitral Annulus Disjunction Arrhythmic Syndrome. *J. Am. Coll. Cardiol.* **2018**, *72*, 1600–1609. [CrossRef] [PubMed]
7. Basso, C.; Iliceto, S.; Thiene, G.; Perazzolo Marra, M. Mitral Valve Prolapse, Ventricular Arrhythmias, and Sudden Death. *Circulation* **2019**, *140*, 952–964. [CrossRef] [PubMed]
8. Essayagh, B.; Sabbag, A.; Antoine, C.; Benfari, G.; Batista, R.; Yang, L.-T.; Maalouf, J.; Thapa, P.; Asirvatham, S.; Michelena, H.; et al. The Mitral Annular Disjunction of Mitral Valve Prolapse: Presentation and Outcome. *JACC Cardiovasc. Imaging* **2021**, *14*, 2073–2087. [CrossRef] [PubMed]
9. Han, H.-C.; Ha, F.J.; Teh, A.W.; Calafiore, P.; Jones, E.F.; Johns, J.; Koshy, A.N.; O'Donnell, D.; Hare, D.L.; Farouque, O.; et al. Mitral Valve Prolapse and Sudden Cardiac Death: A Systematic Review. *J. Am. Heart Assoc.* **2018**, *7*, e010584. [CrossRef] [PubMed]
10. Nalliah, C.J.; Mahajan, R.; Elliott, A.D.; Haqqani, H.; Lau, D.H.; Vohra, J.K.; Morton, J.B.; Semsarian, C.; Marwick, T.; Kalman, J.M.; et al. Mitral valve prolapse and sudden cardiac death: A systematic review and meta-analysis. *Heart* **2019**, *105*, 144–151. [CrossRef] [PubMed]
11. Perazzolo Marra, M.; Basso, C.; Lazzari, M.; Rizzo, S.; Cipriani, A.; Giorgi, B.; Lacognata, C.; Rigato, I.; Migliore, F.; Pilichou, K.; et al. Morphofunctional Abnormalities of Mitral Annulus and Arrhythmic Mitral Valve Prolapse. *Circ. Cardiovasc. Imaging* **2016**, *9*, e005030. [CrossRef] [PubMed]
12. Muthukumar, L.; Rahman, F.; Jan, M.F.; Shaikh, A.; Kalvin, L.; Dhala, A.; Jahangir, A.; Tajik, A.J. The Pickelhaube Sign: Novel Echocardiographic Risk Marker for Malignant Mitral Valve Prolapse Syndrome. *JACC Cardiovasc. Imaging* **2017**, *10*, 1078–1080. [PubMed]

13. Chivulescu, M.; Aabel, E.W.; Gjertsen, E.; Hopp, E.; Scheirlynck, E.; Cosyns, B.; Lyseggen, E.; Edvardsen, T.; Lie, Ø.H.; Dejgaard, L.A.; et al. Electrical markers and arrhythmic risk associated with myocardial fibrosis in mitral valve prolapse. *Europace* **2022**, *24*, 1156–1163. [CrossRef] [PubMed]
14. Constant Dit Beaufils, A.-L.; Huttin, O.; Jobbe-Duval, A.; Senage, T.; Filippetti, L.; Piriou, N.; Cueff, C.; Venner, C.; Mandry, D.; Sellal, J.M.; et al. Replacement Myocardial Fibrosis in Patients With Mitral Valve Prolapse: Relation to Mitral Regurgitation, Ventricular Remodeling, and Arrhythmia. *Circulation* **2021**, *143*, 1763–1774. [PubMed]
15. Figliozzi, S.; Georgiopoulos, G.; Lopes, P.M.; Bauer, K.B.; Moura-Ferreira, S.; Tondi, L.; Mushtaq, S.; Censi, S.; Pavon, A.G.; Bassi, I.; et al. Myocardial Fibrosis at Cardiac MRI Helps Predict Adverse Clinical Outcome in Patients with Mitral Valve Prolapse. *Radiology* **2023**, *306*, 112–121. [CrossRef] [PubMed]
16. Tang, X.; Fan, W. The Association Between Late Gadolinium Enhancement by Cardiac Magnetic Resonance and Ventricular Arrhythmia in Patients With Mitral Valve Prolapse: A Systematic Review and Meta-Analysis. *Clin. Cardiol.* **2024**, *47*, e24316. [CrossRef] [PubMed]
17. Sabbag, A.; Essayagh, B.; Barrera, J.D.R.; Basso, C.; Berni, A.; Cosyns, B.; Deharo, J.-C.; Deneke, T.; Di Biase, L.; Enriquez-Sarano, M.; et al. EHRA expert consensus statement on arrhythmic mitral valve prolapse and mitral annular disjunction complex in collaboration with the ESC Council on valvular heart disease and the European Association of Cardiovascular Imaging endorsed by the Heart Rhythm Society, by the Asia Pacific Heart Rhythm Society, and by the Latin American Heart Rhythm Society. *Europace* **2022**, *24*, 1981–2003. [CrossRef] [PubMed]
18. Bonaros, N.; Gollmann-Tepeköylü, C.; Palmen, M.; Ajmone, N.; Delgado, V.; Garbi, M.; Mayr, A.; Pölzl, L.; Marin-Cuartas, M.; Ascione, G.; et al. Mitral Annular Disjunction: A Roadmap for the Surgeon. *Eur. J. Cardio-Thorac. Surg.* **2026**, *68*, ezaf461. [CrossRef] [PubMed]
19. Lodin, K.; Da Silva, C.O.; Wang Gottlieb, A.; Bulatovic, I.; Rück, A.; George, I.; Cohen, D.J.; Braunschweig, F.; Svenarud, P.; Eriksson, M.J.; et al. Mitral annular disjunction and mitral valve prolapse: Long-term risk of ventricular arrhythmias after surgery. *Eur. Heart J.* **2025**, *46*, 2795–2805. [CrossRef] [PubMed]
20. Bichler, M.; Vitanova, K.; Feirer, N.; Goppel, G.; Steiner, K.; Krane, M.; Boehm, J. Pronounced Mitral Annular Disjunction Is Associated With Increased Postoperative Palpitations After Mitral Valve Surgery for Barlow's Disease. *Interdiscip. Cardiovasc. Thorac. Surg.* **2026**, *41*, ivag104. [CrossRef] [PubMed]
21. Suri, R.M.; Clavel, M.-A.; Schaff, H.V.; Michelena, H.I.; Huebner, M.; Nishimura, R.A.; Enriquez-Sarano, M. Effect of Recurrent Mitral Regurgitation Following Degenerative Mitral Valve Repair: Long-Term Analysis of Competing Outcomes. *J. Am. Coll. Cardiol.* **2016**, *67*, 488–498. [PubMed]
22. Brunec-Keller, M.; Scharf, C.; Radulovic, J.; Berdat, P.A.; Attenhofer Jost, C.H.; Vogt, P.; Duru, F.; Caselli, S. Barlow disease: Effect of mitral valve repair on ventricular arrhythmias in 82 patients in a retrospective long-term study. *J. Cardiovasc. Surg.* **2022**, *63*, 514–520. [CrossRef] [PubMed]
23. Ascione, G.; Azzola Guicciardi, N.; Lorusso, R.; Boccellino, A.; Lapenna, E.; Del Forno, B.; Carino, D.; Bisogno, A.; Palmisano, A.; D'Angelo, G.; et al. The impact of mitral valve surgery on ventricular arrhythmias in patients with Barlow's disease: Preliminary results of a prospective study. *Interdiscip. Cardiovasc. Thorac. Surg.* **2023**, *36*, ivad073. [CrossRef] [PubMed]
24. Mboup, W.N.; N'Guyen Ngok, C.; Riviere, J.-F.; Delarche, N. Sudden cardiac death unveiling a mitral annular disjunction in a young man: The role of multimodal cardiac imaging for diagnosis. *J. Cardiol. Cases* **2025**, *31*, 186–188. [CrossRef] [PubMed]
25. Zeppenfeld, K.; Tfelt-Hansen, J.; Riva, M.; Winkel, B.G.; Behr, E.R.; Blom, N.A.; Charron, P.; Corrado, D.; Dagres, N.; de Chillou, C.; et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur. Heart J.* **2022**, *43*, 3997–4126. [CrossRef] [PubMed]
26. Fumagalli, S.; Pieragnoli, P.; Haugaa, K.H.; Potpara, T.S.; Rasero, L.; Ramacciati, N.; Ricciardi, G.; Solimene, F.; Mascia, G.; Mascioli, G.; et al. The influence of age on the psychological profile of patients with cardiac implantable electronic devices: Results from the Italian population in a multicenter study conducted by the European Heart Rhythm Association. *Aging Clin. Exp. Res.* **2018**, *31*, 1219–1226. [CrossRef] [PubMed]
27. Essayagh, B.; Sabbag, A.; El-Am, E.; Cavalcante, J.L.; Michelena, H.I.; Enriquez-Sarano, M. Arrhythmic mitral valve prolapse and mitral annular disjunction: Pathophysiology, risk stratification, and management. *Eur. Heart J.* **2023**, *44*, 3121–3135. [CrossRef] [PubMed]
28. Rajan, D.; Skjelbred, T.; Hadberg Lynge, T.; Tfelt-Hansen, J. Sudden cardiac death and the role of postmortem genetic testing in unexplained cases. *Indian Pacing Electrophysiol. J.* **2025**, *25*, 441–448. [CrossRef] [PubMed]

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