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Isolated Closure versus Mitral Valvuloplasty for Patent Ductus Arteriosus in Patients with Mitral Regurgitation: A Single-Center, Retrospective Study

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Received: 12 February 2026; Accepted: 09 September 2026; Published: 30 September 2026

ABSTRACT: Background: Patent ductus arteriosus (PDA) can cause left-heart volume overload and functional mitral regurgitation (MR), although some patients have structural mitral abnormalities requiring repair. We compared MR and cardiac remodeling after isolated PDA closure and PDA closure combined with mitral valvuloplasty (MVP). **Methods:** This single-center retrospective study included 68 children treated between February 2013 and February 2025: isolated PDA transcatheter occlusion (IPTO, n = 34), isolated PDA surgical ligation (IPSL, n = 20), and PDA ligation with concomitant mitral valvuloplasty (PLMVP, n = 14). Body-size-adjusted cardiac dimensions were analyzed at baseline and discharge, while MR outcomes were assessed at the latest follow-up. Linear mixed-effects models evaluated temporal changes, and Analysis of Covariance (ANCOVA) assessed net MR-area reduction after adjustment for baseline MR area, age, and PDA size. **Results:** PLMVP patients had numerically larger PDA diameters, more severe MR, and greater left-heart enlargement at baseline. All groups showed significant early reverse remodeling and MR reduction ($p < 0.001$), with the greatest immediate MR-area reduction in PLMVP. From discharge to the latest follow-up, adjusted MR area decreased further in IPTO, remained stable in IPSL, and increased numerically in PLMVP but remained below baseline; the group-by-time interaction was not significant ($p = 0.108$). After adjustment, intervention strategy was not independently associated with net MR-area reduction ($p = 0.874$). **Conclusions:** MR improved after interventions involving PDA closure. In patients without structural mitral abnormalities, isolated closure was associated with reverse remodeling and MR regression. In PLMVP patients, improvement reflected the combined effects of PDA closure, volume-overload relief, and anatomically indicated mitral repair. Concomitant MVP should be individualized according to valve morphology.

KEYWORDS: Patent ductus arteriosus; mitral valve; interventional treatment; surgical ligation

1 Introduction

Patent ductus arteriosus (PDA) remains one of the most prevalent congenital heart anomalies in the pediatric population [1,2]. While small, restrictive shunts are often benign, a hemodynamically significant left-to-right shunt induces progressive pulmonary overcirculation and chronic volume overload on the left heart [3,4]. This sustained excessive preload predisposes to left ventricular (LV) dilation and compensatory

eccentric hypertrophy. As the LV geometry becomes increasingly spherical and the left atrium enlarges, the native mitral annulus is inevitably stretched. This progressive annular dilation, coupled with the outward displacement of the papillary muscles and consequent leaflet tethering, may ultimately contribute to mitral regurgitation (MR), which is predominantly functional/secondary in patients without intrinsic mitral valve abnormalities [5,6].

The optimal management strategy for pediatric patients presenting with PDA complicated by moderate-to-severe MR remains a subject of intense and ongoing clinical controversy [5,7,8]. Although the principal focus of this study was PDA-associated functional/secondary MR, some patients also had intrinsic mitral valve morphological abnormalities. In these patients, PDA-related left-heart volume overload may further aggravate MR, and concomitant MVP may be indicated according to the valve anatomy. One established school of thought advocates for concomitant PDA ligation and surgical mitral valvuloplasty (MVP). The primary advantage of this aggressive approach is the immediate and comprehensive anatomical correction of the incompetent valve, theoretically preventing the long-term hemodynamic burden of chronic MR [8]. However, this strategy is highly invasive, necessitating cardiopulmonary bypass and cardioplegic arrest. Furthermore, surgical manipulation of the pediatric mitral apparatus—often performed without rigid annuloplasty rings to preserve somatic growth potential—carries substantial risks, including future geometric mismatch, delayed progressive mitral stenosis, and an elevated likelihood of challenging reoperations [9,10]. Conversely, in patients without intrinsic mitral valve abnormalities, an alternative, conservative strategy emphasizes the functional/secondary contribution of PDA-related volume overload to MR. Proponents of isolated PDA closure argue that eliminating the ductal shunt effectively eradicates the underlying hemodynamic culprit [5,7]. By completely offloading the left heart, this strategy relies on the robust intrinsic capacity of the growing pediatric myocardium to undergo spontaneous reverse remodeling, allowing the mitral annulus to shrink and leaflet coaptation to be naturally restored without the morbidities associated with concurrent valvular intervention [11,12].

Despite the strong physiological rationale for the conservative approach, definitive empirical evidence comparing the longitudinal outcomes of these two distinct strategies is scarce. Given the relatively elevated surgical risks and the uncertain long-term durability of pediatric MVP, determining whether concurrent valvuloplasty offers any true additive benefit over isolated shunt closure is of paramount clinical relevance [13,14]. Therefore, the aim of this study was to comprehensively evaluate the longitudinal impact of isolated PDA closure compared with combined PDA closure and concurrent MVP. By retrospectively analyzing a decade of institutional data, we sought to delineate the trajectories of left heart reverse remodeling and compare the definitive net regression of MR, thereby providing robust evidence to refine surgical decision-making for this specific cohort.

2 Materials and Methods

2.1 Study Population

In this retrospective, single-center cohort study, we queried our institutional database to identify pediatric patients (<18 years of age) who were clinically diagnosed with both patent PDA and MR and underwent intervention for a PDA complicated by concurrent MR between February 2013 and February 2025. Patients were excluded if they had: (1) other major congenital heart defects requiring surgical correction (except for clinically insignificant atrial or ventricular septal defects); (2) connective tissue disorders (e.g., Marfan syndrome); or (3) active infective endocarditis.

Eligible patients were stratified into three groups based on the actual intervention received, which was determined by a multidisciplinary heart team depending on the patient's age, PDA morphology, and the anatomical severity of the mitral valve apparatus:

The isolated PDA transcatheter occlusion group (IPTO, $n = 34$): Patients who underwent percutaneous transcatheter PDA closure. The isolated PDA surgical ligation group (IPSL, $n = 20$): Patients who underwent isolated surgical PDA ligation or division without concomitant mitral valve intervention. The PDA ligation with mitral valvuloplasty group (PLMVP, $n = 14$): Patients who underwent surgical PDA closure combined with concurrent MVP due to intrinsic structural abnormalities requiring repair (e.g., cleft mitral valve or other leaflet/chordal abnormalities).

The study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (Grant number: KY2025-105-01, February 2024) and adhered to the ethical requirements of the Declaration of Helsinki. Consent forms from patients under eighteen years old were signed by the parents or legal guardians. This study utilized only de-identified historical medical data and information from phone or outpatient interviews, without any additional imaging or laboratory examinations.

2.2 Data Collection and Definition

Comprehensive clinical data were extracted from electronic medical records, including demographic characteristics, baseline clinical status (e.g., New York Heart Association (NYHA) functional class), procedural details, and postoperative outcomes. NYHA functional class was retrospectively determined from documented clinical assessments and caregiver-reported symptoms in the medical records. Class I indicated no limitation of physical activity; Class II indicated slight limitation, with ordinary activity causing symptoms; and Class III indicated marked limitation, with less-than-ordinary activity causing symptoms. Echocardiographic data were the primary focus of this study. Moderate-to-severe pulmonary arterial hypertension (PAH) was assessed by echocardiography. Estimated systolic pulmonary artery pressure (sPAP) was calculated as $4 \times \text{peak tricuspid regurgitation velocity}^2$ plus estimated right atrial pressure. Moderate PAH was defined as an estimated sPAP of 50–70 mmHg, and severe PAH as an estimated sPAP of >70 mmHg; therefore, $\text{PAH} \geq \text{moderate}$ was defined as an estimated sPAP ≥ 50 mmHg. To accurately capture the longitudinal hemodynamic evolution and reverse remodeling of the heart, echocardiographic parameters were collected at three distinct time points: baseline (pre-intervention), at discharge (early post-intervention), and at the latest follow-up. Early post-intervention echocardiography was defined as the last inpatient transthoracic echocardiographic examination performed after the patient had returned to the ward and achieved clinical stability, usually on the day before hospital discharge. Because the timing of discharge varied according to the clinical course, the examination was not scheduled on a fixed postoperative day. The latest follow-up was defined as the most recent available echocardiographic examination after hospital discharge. Follow-up duration was calculated from the date of intervention to the date of this examination. Because follow-up was conducted as part of routine clinical care, its timing was not prespecified and varied among patients. Consistent with the temporal physiological response, structural dimensions including left ventricular end-diastolic diameter (LVEDD), left atrial (LA) diameter, ascending aorta (AAO) diameter, and pulmonary artery (PA) size were evaluated at baseline, discharge, and follow-up. To account for body-size-related variation, Z-scores for LA, LVEDD, left ventricular end-systolic diameter (LVESD), right atrial (RA), PA, and AAO were calculated using the Boston Children's Hospital Z-Score Calculator (<https://zscore.chboston.org/>) [15], with the measurement-specific regression equation selected according to the corresponding echocardiographic parameter and body surface area, follow-up Z-scores were not calculated because height and weight data were incomplete. The severity of MR was

assessed using the absolute regurgitant jet area (MR Area, cm^2) as a continuous variable and MR Grade as a categorical variable. MR Grade was assigned primarily according to MR Area indexed to body surface area ($<4 \text{ cm}^2/\text{m}^2$, mild; $4\text{--}10 \text{ cm}^2/\text{m}^2$, moderate; and $>10 \text{ cm}^2/\text{m}^2$, severe), and $\text{MR} \geq \text{moderate}$ was defined as $\text{MR Grade} \geq 2.0$. Both measures were longitudinally tracked at baseline, discharge, and follow-up. All MR-related echocardiographic measurements were obtained using the standard apical four-chamber view. Measurements were averaged over 3–5 consecutive cardiac cycles. Multiple echocardiographers were involved across the study cohort; for each patient, the measurements were performed by one physician, while MR severity was reviewed by another physician. Formal inter-observer and intra-observer variability analyses were not performed.

2.3 Statistical Analysis

Continuous variables were initially assessed for normality using the Shapiro-Wilk test and visual inspection of Q-Q plots. Given the presence of non-normally distributed data and small sample sizes in certain subgroups (particularly Group 3), continuous variables are presented uniformly as medians with interquartile ranges (IQR). Categorical variables are expressed as frequencies and percentages. To address the treatment-selection bias inherent in the retrospective design (baseline inequalities among the three groups), rigorous statistical adjustments were employed:

Baseline Comparisons: Continuous baseline characteristics were compared using the Kruskal-Wallis H test, followed by Dunn's *post-hoc* test with Bonferroni correction for pairwise comparisons. Categorical variables were compared using the Fisher-Freeman-Halton exact test to strictly account for expected cell counts of less than 5.

Longitudinal Reverse Remodeling: A Linear Mixed-Effects Model (LMM) was constructed to analyze the longitudinal evolution of LA, LVEDD, LVESD, RA, AAO, and PA Z-scores, as well as MR Area. The model incorporated *Time*, *Group*, and their interaction (*Group*Time*) as fixed effects, and a random intercept for each patient to account for within-subject correlation. To reduce confounding from measured baseline differences, the model was adjusted for predefined baseline covariates, including age, PDA size, baseline NYHA class, and the presence of moderate-to-severe pulmonary arterial hypertension. These covariates were selected based on their clinical relevance and potential associations with treatment allocation and cardiac remodeling: age and PDA size reflect developmental status and shunt-related volume load, whereas NYHA class, respiratory infection history, and moderate-to-severe pulmonary arterial hypertension reflect baseline clinical and hemodynamic disease severity. Data derived from the LMM are reported as estimated marginal means $\pm$ standard error (SE).

Analysis of Net Reduction: To evaluate the definitive net improvement in MR, the absolute reduction in MR area (ΔMR , calculated as baseline minus follow-up) was compared among groups using Analysis of Covariance (ANCOVA), with baseline MR area, age, and PDA size entered as covariates.

All statistical analyses were performed using SPSS Statistics, version 31.0 (IBM Corp., Armonk, NY, USA). A two-sided *p*-value of <0.05 was considered statistically significant for main effects, while a Bonferroni-adjusted threshold was applied for *post-hoc* multiple comparisons.

3 Results

3.1 Baseline Characteristics and Treatment-Selection Bias

A total of 68 pediatric patients were included in this study, comprising 34 in IPTO Group, 20 in IPSL Group, and 14 in PLMVP Group. Baseline demographic and clinical characteristics are summarized in Table 1. Consistent with the real-world, non-randomized nature of this cohort, significant treatment-selection bias

was observed at baseline. Patients in PLMVP Group had more severe baseline MR and greater left-heart enlargement than the other groups, whereas PDA diameter differed numerically but not significantly among the three groups ($p = 0.053$). The distribution of sex and the incidence of respiratory infections were comparable across all groups. The median echocardiographic follow-up duration was 348 days (IQR, 97.0–850.5) in the IPTO group, 365 days (IQR, 75.5–823.3) in the IPSL group, and 837 days (IQR, 169.0–1507.5) in the PLMVP group. Follow-up duration did not differ significantly among the three groups ($p = 0.314$).

3.2 Longitudinal Reverse Remodeling of Cardiac Structures

To account for the inherent baseline inequalities, LMMs were utilized to evaluate the longitudinal trajectories of cardiac reverse remodeling, adjusting for baseline PDA size, age, NYHA class, and the presence of moderate-to-severe PAH (Table 2).

Following the elimination of the left-to-right shunt, a highly significant overall reduction was observed in LVEDD and LA size across the entire cohort (Main effect of Time, $p < 0.001$). Notably, the trajectories of reverse remodeling differed significantly among the intervention strategies. The interaction between treatment group and time was highly significant for both LVEDD ($p = 0.010$) and LA diameter ($p = 0.008$). Estimated marginal means revealed that while all groups experienced structural regression, Group 3 demonstrated the steepest reduction trajectory, reflecting a dramatic anatomical response following concurrent intervention on the mitral apparatus.

3.3 Evolution and Trajectories of Mitral Regurgitation Severity

The longitudinal evolution of MR was assessed at three critical junctures: baseline, at discharge (early phase), and at the latest follow-up (Table 2).

In the immediate postoperative period (baseline to discharge), all three groups achieved a substantial reduction in the absolute MR area. PLMVP Group, which had the largest baseline MR area, exhibited a drastic early decline, confirming the immediate mechanical efficacy of concurrent MVP.

However, diverging trajectories were observed during the late follow-up period (discharge to follow-up). While the adjusted MR area in IPTO Group continued to decrease (from 1.220 to 0.721 cm²) and IPSL Group remained largely stable (from 0.956 to 0.899 cm²), PLMVP Group showed a numerical increase in adjusted MR area from discharge to the latest follow-up; however, the MR area remained lower than the baseline value (increasing from 1.918 cm² at discharge to 2.383 cm² at follow-up) (p for Group*Time interaction = 0.108). At the latest available echocardiographic follow-up, residual moderate-to-severe MR was present in 4 of 29 patients (13.8%) in the IPTO group, 2 of 20 patients (10.0%) in the IPSL group, and 5 of 13 patients (38.5%) in the PLMVP group. The overall difference among the three groups was not statistically significant ($p = 0.101$).

Table 1: Baseline characteristics and follow-up duration of all groups.

Items	IPTO (n = 34)	IPSL (n = 20)	PLMVP (n = 14)	<i>p</i> Value _{IPTO-IPSL}	<i>p</i> Value _{IPTO-PLMVP}	<i>p</i> Value _{IPSL-PLMVP}	<i>p</i> Value _{Total}
Gender [Female, n (%)]	29 (85.3)	18 (90.0)	10 (71.4)				0.381
Age (months)	9.5 (5.8, 17.1)	21.5 (13.8, 34.3)	9.5 (4.5, 16.5)	0.008	0.999	0.030	0.005
Weight (kg)	7.0 (4.9, 8.5)	10.0 (8.1, 12.5)	6.5 (4.9, 9.0)	0.02	0.999	0.017	0.001
Height (cm)	67.5 (60.8, 76.3)	83.5 (73.5, 95.0)	66.5 (58.0, 72.5)	0.007	0.999	0.013	0.003
LVEF (%)	70.0 (67.0, 75.8)	70.0 (66.2, 74.3)	73.0 (56.5, 77.3)				0.869
PDA Diameter (mm)	5.9 ± 1.8	4.7 ± 1.6	5.7 ± 1.4				0.053
MR ≥ moderate [n (%)]	20 (58.8)	8 (40.0)	14 (100)	0.781	0.012	<0.001	<0.001
TR ≥ Moderate [n (%)]	1 (2.9)	0	2 (14.3)				0.181
LA Z-Score	3.42 (2.69, 4.54)	2.65 (1.80, 3.83)	3.75 (3.33, 4.12)	0.119	0.931	0.029	0.024
LVEDD Z-Score	5.74 (3.18, 8.20)	4.14 (2.03, 6.18)	7.84 (6.18, 9.13)	0.456	0.130	0.008	0.011
LVESD Z-Score	3.49 (1.83, 5.59)	2.03 (0.83, 4.94)	5.22 (0.58, 9.14)	0.377	0.224	0.013	0.017
RA Z-Score	−4.26 (−4.64, −3.98)	−4.65 (−5.13, −4.27)	−4.20 (−4.82, −3.58)	0.026	0.999	0.047	0.014
AAO Z-Score	0.90 (0.32, 2.10)	0.085 (−0.748, 1.16)	0.53 (−0.62, 1.64)	0.028	0.814	0.808	0.032
PA Z-Score	2.88 (2.11, 4.48)	3.03 (0.45, 4.29)	2.72 (1.10, 3.91)				0.543
Predisposed to Respiratory infection [n (%)]	19 (55.9)	13 (65.0)	10 (71.4)				0.567
PAH ≥ moderate [n (%)]	12 (35.3)	3 (15.0)	9 (64.3)	0.294	0.186	0.015	0.013
NYHA classification [n (%)]				0.057	<0.001	0.012	<0.001
Class I	6 (17.6)	6 (30.0)	0				
Class II	17 (50.0)	14 (70.0)	6 (42.9)				
Class III	11 (32.4)	0	8 (57.1)				
Follow-up duration (days)	348.0 (97.0, 850.5)	365.0 (75.5, 823.3)	837.0 (169.0, 1507.5)	NA	NA	NA	0.314

Data are presented as median [interquartile range, IQR] or mean ± standard deviation (SD) for continuous variables due to non-normal distributions, and as frequencies (percentages) for categorical variables. Continuous variables were compared using the Kruskal-Wallis H test. Categorical variables were compared using the Fisher-Freeman-Halton exact test due to expected cell counts of less than 5. A Bonferroni-adjusted significance level was applied for all *post-hoc* pairwise comparisons. MR ≥ moderate includes moderate, moderate-to-severe, and severe MR. Moderate-to-severe pulmonary hypertension was defined as echocardiographically estimated systolic pulmonary artery pressure ≥50 mmHg. NYHA functional classes I–III were defined as described in 2.2 Data Collection and Definition. Follow-up duration was calculated from the date of intervention to the latest available echocardiographic examination. Abbreviations: PDA, patent ductus arteriosus; IPTO, isolated PDA transcatheter occlusion; IPSL, isolated PDA surgical ligation; PLMVP, PDA ligation combined with mitral valvuloplasty; PAH, pulmonary arterial hypertension; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; TR, tricuspid regurgitation; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; RA, right atrium; AAO, ascending aorta; PA, pulmonary artery; NYHA, New York Heart Association; NA, not applicable. Pairwise comparisons were performed only when the overall three-group comparison was statistically significant; otherwise, pairwise *p*-value cells were left blank.

Table 2: Longitudinal evolution of echocardiographic parameters.

Variables	Time Point	IPTO (n = 34)	IPSL (n = 20)	PLMVP (n = 14)	P_{Group}	P_{Time}	$P_{\text{Interaction}}$
LA Z-score	Baseline	3.309 ± 0.200	3.016 ± 0.284	3.564 ± 0.447	0.199	<0.001	0.008
	Discharge	1.453 ± 0.256	1.976 ± 0.348	3.022 ± 0.670			
LVEDS Z-score	Baseline	3.761 ± 0.463	3.329 ± 0.661	5.324 ± 0.989	0.835	0.007	0.086
	Discharge	2.923 ± 0.610	3.207 ± 0.830	2.609 ± 1.268			
LVEDD Z-score	Baseline	5.560 ± 0.512	5.314 ± 0.731	7.506 ± 1.094	0.886	<0.001	0.010
	Discharge	2.341 ± 0.600	2.634 ± 0.831	1.559 ± 1.260			
RA Z-score	Baseline	-4.405 ± 0.080	-4.440 ± 0.107	-4.186 ± 0.138	0.122	0.164	0.458
	Discharge	-4.239 ± 0.061	-4.445 ± 0.086	-4.016 ± 0.670			
AAO Z-score	Baseline	0.967 ± 0.221	0.367 ± 0.308	0.219 ± 0.466	0.205	0.566	0.737
	Discharge	0.902 ± 0.227	0.444 ± 0.316	0.545 ± 0.478			
PA Z-score	Baseline	3.217 ± 0.341	3.041 ± 0.473	2.672 ± 0.717	0.365	<0.001	0.455
	Discharge	1.785 ± 0.327	1.807 ± 0.457	0.426 ± 0.690			
MR Area (cm²)	Baseline	1.926 ± 0.241	1.625 ± 0.352	3.454 ± 0.500	0.043	<0.001	0.108
	Discharge	1.220 ± 0.261	0.956 ± 0.376	1.918 ± 0.540			
	Follow-up	0.721 ± 0.284	0.899 ± 0.391	2.383 ± 0.585			
Residual MR ≥ moderate [n (%)]	Discharge	10 (29.4)	3 (15)	6 (42.9)	0.217	NA	NA
	Follow-up	4 (13.8)	2 (10)	5 (38.5)			

PDA, patent ductus arteriosus; IPTO, isolated PDA transcatheter occlusion; IPSL, isolated PDA surgical ligation; PLMVP, PDA ligation combined with mitral valvuloplasty; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVEDS, left ventricular end-systolic diameter; RA, right atrium; AAO, ascending aorta; PA, pulmonary artery; MR, mitral regurgitation; NA, not applicable. Data for continuous variables, including LA, LVEDD, LVEDS, RA, AAO, and PA Z-scores and MR Area, are presented as estimated marginal means ± standard error (SE) derived from linear mixed-effects models (LMMs). Follow-up Z-scores were not calculated because height and weight data at follow-up were incomplete. Therefore, Z-score models included baseline and discharge, whereas the MR Area model included baseline, discharge, and the latest follow-up. To adjust for significant baseline treatment-selection bias, all models were evaluated with covariates held constant at the following overall mean values: [New York Heart Association (NYHA) class = 2.05, PDA diameter = 5.43 mm, and age = 16.57 months, and the moderate-to-severe pulmonary arterial hypertension (PAH) indicator = 0.27. Moderate-to-severe PAH was coded as 0 (absent) and 1 (present); therefore, a mean of 0.27 corresponds to a prevalence of 27% in the analysis sample]. Longitudinal analysis confirmed rapid and durable recovery. For categorical MR outcomes, data are presented as n/N (%), where N represents patients with an available MR assessment at the specified time point. Overall between-group p values were calculated using the Fisher-Freeman-Halton exact test and were not derived from the linear mixed-effects models.

3.4 Adjusted Net Reduction in MR Area

To assess whether intervention strategy was associated with net MR-area reduction after accounting for baseline differences, Δ MR from baseline to follow-up was analyzed using ANCOVA (Table 3). Of the 62 patients with follow-up MR assessments, 61 had available Δ MR values and were included in the ANCOVA; one patient was excluded because Δ MR was missing. The overall corrected model was significant ($F(5, 55) = 6.776$, $p < 0.001$; $R^2 = 0.381$; adjusted $R^2 = 0.325$). A larger baseline MR area was associated with a greater net reduction in MR ($B = 0.568$, 95% confidence interval (CI): 0.317 to 0.818; $p < 0.001$), whereas older age at intervention was associated with a smaller net reduction ($B = -0.033$ per month, 95% CI: -0.060 to -0.007 ; $p = 0.014$). PDA size was not independently associated with net MR-area reduction ($B = -0.079$, 95% CI: -0.301 to 0.142 ; $p = 0.474$). After adjustment, intervention strategy was not independently associated with net MR-area reduction ($F(2, 55) = 0.135$; $p = 0.874$; partial $\eta^2 = 0.005$). Given treatment-selection bias and the structural mitral pathology in the PLMVP group, the independent contributions of PDA closure and MVP could not be separated.

Table 3: Analysis of covariance for net reduction in mitral regurgitation area (Δ MR) after intervention.

Panel A. Tests of between-Subjects Effects						
Source	Type III SS	df*	Mean Square	F	p	Partial η^2
Corrected model	57.715	5/55	11.543	6.776	<0.001	0.381
Intercept	3.580	1/55	3.580	2.102	0.153	0.037
Intervention strategy	0.459	2/55	0.229	0.135	0.874	0.005
Baseline MR area	35.135	1/55	35.135	20.625	<0.001	0.273
Age at intervention	10.988	1/55	10.988	6.45	0.014	0.105
PDA size	0.884	1/55	0.884	0.519	0.474	0.009
Error	93.695	55	1.704	—	—	—
Total	243.869	61	—	—	—	—
Corrected total	151.410	60	—	—	—	—
Panel B. Parameter Estimates						
Parameter	B	SE	t	p	95% CI	Partial η^2
Intercept	0.870	0.841	1.035	0.305	−0.815 to 2.556	0.019
IPTO vs. PLMVP	0.024	0.509	0.047	0.963	−0.996 to 1.043	0.000
IPSL vs. PLMVP	0.237	0.593	0.400	0.69	−0.950 to 1.425	0.003
Baseline MR area	0.568	0.125	4.541	<0.001	0.317 to 0.818	0.273
Age at intervention (months)	−0.033	0.013	−2.540	0.014	−0.060 to −0.007	0.105
PDA size (mm)	−0.079	0.110	−0.720	0.474	−0.301 to 0.142	0.009
Panel C. Adjusted Marginal Means for ΔMR by Intervention Strategy						
Intervention Group	Adjusted Mean ΔMR	SE	95% CI			
IPTO	1.166	0.253	0.659–1.673			
IPSL	1.379	0.331	0.716–2.043			
PLMVP	1.142	0.436	0.268–2.016			

Δ MR was calculated as baseline MR area minus follow-up MR area; positive values indicate a greater net reduction. Analysis of Covariance (ANCOVA) included 61 complete cases and adjusted for baseline MR area, age at intervention, and PDA size; one of the 62 patients with follow-up MR assessments was excluded because Δ MR was missing. *For F tests, degrees of freedom (df) values are presented as numerator/denominator degrees of freedom. The overall model had $R^2 = 0.381$ (adjusted $R^2 = 0.325$). Group 3 was the reference category. B, unstandardized coefficient; CI, confidence interval; MR, mitral regurgitation; PDA, patent ductus arteriosus; IPTO, isolated PDA transcatheter occlusion; IPSL, isolated PDA surgical ligation; PLMVP, PDA ligation combined with mitral valvuloplasty; SE, standard error; SS, sum of squares; η^2 , Eta squared.

4 Discussion

The optimal management strategy for PDA complicated by concurrent moderate-to-severe MR in pediatric patients remains a subject of clinical debate. This study longitudinally evaluated the morphological and hemodynamic evolution of the left heart following three distinct intervention strategies. Our principal findings demonstrate that: (1) elimination of the ductal shunt, regardless of the approach, triggers profound reverse remodeling of the left heart chambers; (2) while concurrent MVP yields immediate morphological benefits, intervention strategy was not independently associated with net MR-area reduction after adjustment for baseline disease severity; and (3) isolated closure strategies (both interventional and surgical) were associated with continued late improvement in valve competence, supporting a parsimonious, wait-and-see approach for the mitral apparatus in this specific patient population.

4.1 The Physiology of Reverse Remodeling and Secondary MR

The underlying pathophysiology of MR in the context of an isolated large PDA is predominantly functional, driven by chronic left-to-right shunting leading to left atrial and ventricular volume overload,

annular dilatation, and subsequent leaflet tethering [7,16,17]. Our LMM analysis revealed a highly significant temporal regression in both LVEDD and LA size across all cohorts following intervention. This confirms that once the excess volume burden is eradicated, the pediatric myocardium possesses a robust capacity for geometric restoration [18]. Consequently, mitigating annular dilatation directly facilitates spontaneous improvement in leaflet coaptation, as observed in our isolated closure groups, where MR area continued to regress steadily from discharge through late follow-up.

4.2 Interpretation of MR Outcomes in the PLMVP Group

The PLMVP group exhibited the greatest immediate reduction in MR area at discharge, consistent with the early effect of anatomically indicated mitral repair combined with PDA closure. At the latest follow-up, the adjusted MR area was numerically higher than that at discharge but remained lower than the baseline value. This pattern should therefore be interpreted as sustained overall improvement relative to baseline, rather than definitive late MR rebound or deterioration. As the group-by-time interaction was not statistically significant, the observed numerical difference between discharge and follow-up should be interpreted cautiously. The PLMVP group comprised patients with intrinsic mitral structural abnormalities requiring concomitant repair and should not be considered a purely functional-MR cohort [19]. In these patients, chronic PDA-related volume overload may coexist with and aggravate MR caused by structural mitral pathology. Accordingly, the postoperative change in MR reflects the combined effects of PDA closure, relief of left-heart volume overload, and anatomically indicated mitral repair [14,20]. The small sample size, heterogeneity of structural lesions and repair techniques, changes in loading conditions, and somatic growth may influence the numerical difference between discharge and latest follow-up. However, the present study was not designed to determine the independent contribution or long-term durability of each component of the combined treatment. Importantly, because MR remained lower than baseline at follow-up, these data do not support the conclusion that concomitant MVP is counterproductive.

4.3 Addressing Treatment-Selection Bias and True Net Benefit

A critical challenge in evaluating these therapeutic strategies is the inherent treatment-selection bias; in our cohort, concurrent MVP was exclusively reserved for patients with the most extreme baseline annular dilatation and the largest MR areas. To untangle this bias, we utilized an ANCOVA model to assess the net reduction in MR area (Δ MR). After adjustment for baseline MR area, age, and PDA size, intervention strategy was not independently associated with the net reduction in MR area. However, because patients in the PLMVP group had structural mitral abnormalities, a fundamentally different pathophysiology from the functional MR in the IPTO and IPSL groups, this statistical finding should not be interpreted as evidence that isolated closure is equivalent to concurrent MVP in patients with structural mitral pathology.

4.4 Clinical Implications

These findings have important implications for surgical decision-making. In children without intrinsic mitral structural abnormalities, isolated PDA closure may be followed by substantial and sustained improvement in MR through relief of left-heart volume overload and reverse remodeling. Importantly, the presence of structural mitral pathology should not preclude PDA closure. In our PLMVP cohort, MR remained lower at the latest follow-up than at baseline, indicating sustained overall improvement after PDA closure combined with anatomically indicated mitral repair. However, because these patients underwent concomitant MVP, the independent contribution of PDA closure cannot be separated from that of mitral

repair. Therefore, concomitant mitral intervention should be individualized according to valve morphology rather than routinely performed solely on the basis of MR severity.

5 Limitations

This study has several limitations. First, the retrospective, single-center design and the lack of standardized criteria for treatment allocation introduce inherent selection bias. Although robust mixed-effects and covariance models were utilized to mitigate these baseline imbalances, unmeasured confounding may remain. Second, the small sample size in the PLMVP group ($n = 14$) limits the statistical power of our analyses. Third, the study did not standardize or adjust for concomitant medical therapy (e.g., diuretics, afterload reduction) that could influence MR severity. Fourth, the lack of routine three-dimensional echocardiography precludes detailed biomechanical assessment of mitral valve anatomy and function. Fifth, the study did not collect data on symptomatic status, exercise capacity, or quality of life, which are important patient-centered outcomes. Sixth, follow-up timing was not standardized, and incomplete follow-up height and weight data prevented calculation of body-size-adjusted chamber Z-scores, limiting assessment of longer-term structural remodeling and late MVP complications. Finally, the findings represent the experience of a single high-volume center with expertise in pediatric cardiac surgery and interventional cardiology. The generalizability of these results to lower-volume centers or to populations with different patient demographics may be limited. Future large-scale, prospective studies are warranted to validate these findings and refine patient selection criteria.

6 Conclusions

In pediatric patients with PDA complicated by moderate-to-severe MR, MR improved following interventions that included PDA closure and remained lower than baseline at latest follow-up, both in patients managed with isolated ductal closure and in those requiring PDA closure combined with concomitant MVP for intrinsic mitral structural abnormalities. In patients without structural mitral abnormalities, isolated ductal closure was associated with regression of left heart enlargement and improvement in MR. In patients with structural mitral pathology, improvement should be interpreted as the combined effect of PDA closure, relief of volume overload, and anatomically indicated mitral repair. Therefore, intrinsic mitral abnormalities should not preclude PDA closure, whereas the need for concomitant MVP should be individualized according to valve morphology. Given the underlying differences between patient groups and the small sample size, the independent contribution of MVP versus isolated PDA closure cannot be definitively determined from this retrospective study.

Acknowledgement: Not applicable.

Funding Statement: This research was funded by the Natural Science Foundation of Guangdong Province (grant number: 2023A1515012501) and Guangdong Special Funds for Science and Technology Innovation Strategy, China (Stability support for scientific research institutions affiliated to Guangdong Province-GDCI 2023) (grant number: KD022023019).

Author Contributions: The authors confirm contribution to the paper as follows: conceptualization, Haiyun Yuan; methodology, Xiaohua Li and Jiaqing Tang; software, Jiaqing Tang and Yushen Fang; validation, Haiyun Yuan and Xiaohua Li; formal analysis, Zhuyang Yang and Huiru Xie; investigation, Zechen Li and Jiahong Li; resources, Haiyun Yuan, Xiaohua Li and Zhanhao Su; data curation, Miao Tian; writing—original draft preparation, Jiaqing Tang; writing—review and editing, Shusheng Wen and Haiyun Yuan; supervision, Xiaohua Li and Haiyun Yuan; project administration and funding acquisition, Haiyun Yuan. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials: The data of this study were available from the corresponding authors upon reasonable request.

Ethics Approval: The study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (Grant number: KY2025-105-01, February 2024) and adhered to the ethical requirements of the Declaration of Helsinki. Consent forms from patients under eighteen years old were signed by the parents or legal guardians. This study utilized only de-identified historical medical data and information from phone or outpatient interviews as part of routine clinical follow-up.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, et al. Global birth prevalence of congenital heart defects 1970–2017: updated systematic review and meta-analysis of 260 studies. *Int J Epidemiol*. 2019;48(2):455–63. [[CrossRef](#)].
2. Xu J, Li Q, Deng L, Xiong J, Cheng Z, Ye C. Global, regional, and national epidemiology of congenital heart disease in children from 1990 to 2021. *Front Cardiovasc Med*. 2025;12:1522644. [[CrossRef](#)].
3. Writing Committee, Sachdeva R, Parthiban A, Birnbaum B, Hancock HS, Jayaram NM, et al. Outpatient management of isolated left-to-right shunt lesions in pediatric patients: 2026 ACC concise clinical guidance: a report of the American college of cardiology solution set oversight committee. *J Am Coll Cardiol*. 2026;87(22):3185–206. [[CrossRef](#)].
4. Baruteau AE, Méot M, Benbrik N, Grunenwald C, Lwin N, Patkai J, et al. Device closure of hemodynamically significant patent ductus arteriosus in premature infants. *JACC Adv*. 2024;3(10):101211. [[CrossRef](#)].
5. Schneider DJ. The patent ductus arteriosus in term infants, children, and adults. *Semin Perinatol*. 2012;36(2):146–53. [[CrossRef](#)].
6. Almomani ASA, Khassawneh MH, Almomanie AF, Alqusur QKJ, Alkhazaleh AH. Transcatheter closure of patent ductus arteriosus with mitral regurgitation in children: clinical outcome and improvement of mitral regurgitation after procedure with echocardiogram follow-up. *World J Bio Pharm Health Sci*. 2024;20(2):476–83. [[CrossRef](#)].
7. Bhuvaneswaran Kartha G, Irene Varghese S, Krupa J, George Alex A, George OK, Samuel Thomson V. Fate of mitral regurgitation after transcatheter closure of patent ductus arteriosus: single centre study. *Indian Heart J*. 2025;77(3):231–4. [[CrossRef](#)].
8. Yao M, Ren C, Ye W. Surgical treatment for large ductus arteriosus with functional mitral regurgitation in children. *Acad J Chin PLA Med Sch*. 2021;42(1):57–60.
9. Isaacson E, Lucjak C, Johnson WK, Yin Z, Wang T, Rein L, et al. Mitral valve surgery in neonates, infants, and children: surgical approach, outcomes, and predictors. *Semin Thorac Cardiovasc Surg*. 2020;32(3):541–50. [[CrossRef](#)].
10. Fu H, Liu A, Yang M, Liu Z, Su J. Midterm outcomes of pediatric mitral valvuloplasty for moderate to severe mitral valve regurgitation and associated risk factors for postoperative deterioration. *Tex Heart Inst J*. 2025;52(2):e248523. [[CrossRef](#)].
11. Kheiwa A, Ross RD, Kobayashi D. Reversal of severe mitral regurgitation by device closure of a large patent ductus arteriosus in a premature infant. *Cardiol Young*. 2017;27(1):189–92. [[CrossRef](#)].
12. Gupta SK, Krishnamoorthy K, Tharakan JA, Sivasankaran S, Sanjay G, Bijulal S, et al. Percutaneous closure of patent ductus arteriosus in children: immediate and short-term changes in left ventricular systolic and diastolic function. *Ann Pediatr Cardiol*. 2011;4(2):139–44. [[CrossRef](#)].
13. Zhang H, Gu C, Shentu J, Li G, Xiao T, Zhu Z, et al. Development and validation of a novel score to predict adverse outcomes in paediatric congenital mitral regurgitation (PRIMARY): a multicentre cohort study. *EClinicalMedicine*. 2025;88:103477. [[CrossRef](#)].
14. Ando M, Takahashi Y. Durability of mitral valve repair performed before the age of 5 years. *Circ J*. 2016;80(1):124–9. [[CrossRef](#)].
15. Boston Children's Hospital. Z-score calculator [Internet]. Boston, MA, USA: Boston Children's Hospital; 2026 [cited 2026 Jun 25]. Available from: <https://zscore.chboston.org/>.

16. D'Ancona G, Kische S, Agha HU, Ince H. Treatment of secondary mitral valve regurgitation: why we need combined and evolving percutaneous strategies to tackle this moving target. *EuroIntervention*. 2015;11(Suppl W):W49–52. [[CrossRef](#)].
17. Ong HS, Krishnasamy S, Rajandram R, Amirthalingam A, Yusof TNT, Sivalingam S. Moderate mitral regurgitation in association with ventricular septal defect in children: does it warrant mitral valve repair? *Ann Pediatr Cardiol*. 2024;17(4):264–71. [[CrossRef](#)].
18. Khajali Z, Firouzi A, Shakerian F, Alemzadeh-Ansari MJ, Ghobadi E, Khalilipour E, et al. Cardiac reverse remodeling after transcatheter patent ductus arteriosus closure in adults. *Curr Probl Cardiol*. 2022;47(10):100938. [[CrossRef](#)].
19. Chen W, Li M, Sheng W, Jia B, Huang G. Congenital mitral valve defects in pediatric population: a narrative review of surgical repair. *Pediatr Med*. 2023;6:6. [[CrossRef](#)].
20. Amin S, Dewey H, Lasso A, Sabin P, Han Y, Vicory J, et al. Euclidean and shape-based analysis of the dynamic mitral annulus in children using a novel open-source framework. *J Am Soc Echocardiogr*. 2024;37(2):259–67. [[CrossRef](#)].