Cardiology in the Young

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Surgical outcomes of double-orifice mitral valve repair in patients with atrioventricular canal defects: a systematic review and meta-analysis

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Review

Cite this article: Ghosh S, Halder V, Mittal A, Mishra A, Haranal M, Aggarwal P, Singh H, Barwad P, Naganur S, and Thingnam SKS (2023) Surgical outcomes of double-orifice mitral valve repair in patients with atrioventricular canal defects: a systematic review and meta-analysis. *Cardiology in the Young* **33**: 1506–1516. doi: 10.1017/S1047951123002664

Received: 1 June 2023
Revised: 28 June 2023
Accepted: 29 June 2023
First published online: 31 July 2023

Keywords:
Double-orifice mitral valve; double-orifice left atrioventricular valve; atrioventricular septal defect; regurgitation; cleft closure

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Abstract

Introduction: Double-orifice mitral valve or left atrioventricular valve is a rare congenital cardiac anomaly that may be associated with an atrioventricular septal defect. The surgical management of double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect is highly challenging with acceptable clinical outcomes. This meta-analysis is aimed to evaluate the surgical outcomes of double-orifice mitral valve/double-orifice left atrioventricular valve repair in patients with atrioventricular septal defect. *Methods and results:* A total of eight studies were retrieved from the literature by searching through PubMed, Google Scholar, Embase, and Cochrane databases. Using Bayesian hierarchical models, we estimated the pooled proportion of incidence of double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect as 4.88% in patients who underwent surgical repair (7 studies; 3295 patients; 95% credible interval [CI] 4.2–5.7%). As compared to pre-operative regurgitation, the pooled proportions of post-operative regurgitation were significantly low in patients with moderate status: 5.1 versus 26.39% and severe status: 5.7 versus 29.38% [8 studies; 171 patients]. Moreover, the heterogeneity test revealed consistency in the data ($p < 0.05$). Lastly, the pooled estimated proportions of early and late mortality following surgical interventions were low, that is, 5 and 7.4%, respectively. *Conclusion:* The surgical management of moderate to severe regurgitation showed corrective benefits post-operatively and was associated with low incidence of early mortality and re-operation.

Double-orifice mitral valve or left atrioventricular valve along with atrioventricular septal defect is a complicated condition with an incidence of about 3–7%.[1] The clinical spectrum of the double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect ranges from an incidental finding during pulmonary banding, autopsy, surgical procedures, or echocardiography, to less frequent presentation with mitral valve regurgitation or stenosis.[2,3] Clinical reports in the literature suggest that patients with double-orifice mitral valve without mitral regurgitation or stenosis are asymptomatic.[4] Therefore, the surgical management of the defect is considerably challenging due to the lack of clinical effects depending on the severity and duration of mitral regurgitation.

Evidence from the literature reports improvement in the clinical outcomes and surgical implications in recent years.[2,5,6] Surgical repair in early infancy is a common practice nowadays.[6,7] However, pre- and post-operative regurgitation, incomplete cleft closure, and associated cardiovascular anomalies remain risk factors of re-operation and mortality.[7] The risk factors are attributed to the presence of an immature or abnormal lateral leaflet, especially in the intermediate or complete type.[8] Since the diseased condition is highly uncommon as represented by fewer studies present in the literature, this meta-analysis is an attempt to review the clinical and surgical experiences to establish the possible outcomes of double-orifice mitral or left AV valve repair in patients with atrioventricular septal defect.

Methods

The meta-analysis follows the guidelines of the Cochrane Handbook and Meta-analysis of Observational Studies in Epidemiology guidelines,[9] which were prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations. A literature search was performed using PubMed, Google Scholar, Embase, and Cochrane databases using the following search keywords in various combinations: "double orifice mitral valve," "surgical repair," "double orifice left atrioventricular valve," "endocardial cushion defect," "atrioventricular septal defect," "valve repair," "atrioventricular canal defect," "DOMV,"

"DOLAVV," "AVSD," and "AVCD." Only English language studies with full publications were considered for this study with no restrictions on publication year.

Inclusion criteria

Clinical trials, observational studies, and retrospective studies that reported the experiences, strategies, and outcomes of surgical repair of double-orifice mitral valve/double-orifice left atrioventricular valve with partial, intermediate, and complete atrioventricular septal defect were included. In addition, studies with inclusive parameters such as patient characteristics, surgical procedures, cleft closure, pre- and post-operative regurgitation, stenosis, mortality, and mean follow-up of a minimum of 1 year were noted.

Exclusion criteria

Case reports, expert opinions, literature reviews, editorials, and conference abstracts were excluded from the study. In addition, studies with missing data on any one of the mentioned parameters and studies associated with only double-orifice tricuspid valves were excluded.

Data extraction

The following variables were noted: study details (sample size, study period, length of follow-up), age, diseased condition (partial, intermediate, or complete atrioventricular septal defect, stenosis, regurgitation), surgical procedures (partial or complete cleft closure), and post-operative data (early or late mortality, incidence of re-operation, post-operative regurgitation).

Statistical analysis

Depending on the availability, the data for clinical outcomes were retrieved from the selected publications or were calculated after extracting the numeric data. The proportions were calculated from the exact number of patients in each group with 95% credible intervals [CI]. The Bayesian hierarchical models were used to estimate the pooled proportion of surgical outcomes and associated factors across studies. The results were depicted using forest plots. We also performed fixed-effects meta-regression of the natural logarithm of the odds ratio for pre- and post-operative regurgitation. Further, heterogeneity tests were performed to estimate the level of inconsistency (I^2) across the selected publications. Lastly, the publication biasness was assessed using Egger's and Begg's tests. Publication bias is considered in a situation when the decision to publish a manuscript depends on statistically significant results. The statistical analysis was performed using MetaXL software.

Results

Search results

Although the literature search resulted in 467 articles, only 39 pertinent studies were identified and included in a full-text review. After close analysis, eight articles were included in the final meta-analysis based on the data of interest (Fig. 1). Among them, five studies were retrospective. The study characteristics and included variables of these publications are summarised in Table 1.

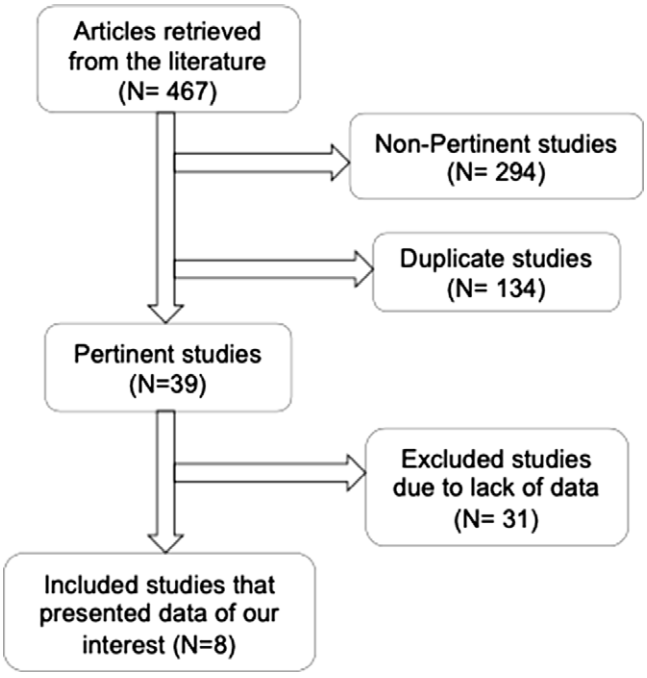

Figure 1. Consort flow diagram.

Incidence of double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect

A total of 3,306 patients who underwent surgical repair were included in the analysis. Among them, only 4.88% of patients showed the incidence of double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect (7 studies, 3,295 patients, 95% CI 4.2–5.7%). The I^2index ($I^2 = 39.76\%$, $p = 0.126$) (Fig. 2) and publication biasness using Egger's test (intercept = 0.67, $p = 0.69$) and Begg's test (Kendall's Tau = 0.143, $p = 0.65$) were found to be non-significant. Egger's and Begg's tests suggested no evidence of asymmetry and small-study effects for the incidence of double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect in selected studies. Further, the data on complete or incomplete double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect were given in 6 studies only. Out of 145 patients, 76 patients showed complete double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect, whereas 69 patients showed incomplete double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect.

Pre- and post-operative regurgitation

The severity of regurgitation ranges from trivial to severe. Based on the severity levels, the data were extracted from the publications, and severity proportions were estimated separately (8 studies; 171 patients). In 8 studies, 154/171 patients represented pre-operative regurgitation, whereas 55/171 patients represented post-operative regurgitation. A significant difference in the regurgitation status was found (OR = 0.08, $p = 0.0002$), as shown in Figure 3.

Further, the pooled proportion results revealed a tremendous decline in the moderate and severe status of post-operative regurgitation in patients as compared to those with pre-operative regurgitation. Moreover, heterogeneity tests revealed consistency

https://doi.org/10.1017/S1047951123002664 Published online by Cambridge University Press

Table 1. Study characteristics and operative outcomes.

S. No.	Parameters	Ohta et al.	Hoohenkerk et al.	Pontailler et al.	Sharma et al.	Pontailler/ Kalfa et al.	Ando et al.	Lee et al.	Warnes et al.
1	Data collection in years	1991–1999	1975–2006	1987–2016	1961–2009	2000–2012	1992–2008	1961–1984	1962–1982
2	Surgical intervention for AVCD/ AVSD	128	312	1067	657	412	138	581	–
3	Age:								
	Range	3–14 y	1.4 m–11.9 y	1 m–30 y	2 m–70 y	1 m–59.7 y	–	3 m–56 y	10 m–20 y
	Mean/Median Age	–	8.2 m	1.3 y	6.6 y	6.9 m	7.1 m	8.3 y	–
4	Clinical stage of AVSD:								
	Complete	82	209	–	–	240	138	253	–
	Partial	33	76	–	–	131	0	321	–
	Intermediate	13	27	–	–	41	0	7	–
5	Sample size (included patients)	5	21	43	44	15	7	25	11
6	DOMV/ DOLAVV + AVSD:	5	21	43	44	15	7	25	11
	Complete	2	9	20	15	–	7	16	–
	Partial	3	9	20	28	–	0	9	–
	Intermediate	0	3	3	1	–	0	0	–
	Incidence	5.40%	6.70%	4%	6.70%	3.60%	5.07%	4.3%	–
7	Pre-operative regurgitation:								
	Mild	0	7	13	0	7	5	0	7
	Moderate	3	10	12	0	6	2	17	2
	Severe	0	4	8	35	2	0	0	2
	Trivial	2	0	10	9	0	0	6	0
8	Regurgitation of accessory orifice	–	14	0	4	–	2	–	–
9	Post-operative regurgitation:								
	Mild	0	3	0	21	0	3	10	0
	Moderate	0	2	6	0	0	0	1	0
	Severe	0	2	2	5	0	0	0	0
	Trivial	5	14	35	17	–	0	10	7
10	LAVV stenosis during follow-up	–	0	–	4	–	0	–	–
11	Mitral stenosis during follow-up	0	–	–	0	–	0	2	–
12	Accessory orifice:								
	Lateral leaflet	2	0	–	–	–	–	–	–
	Posterior leaflet	3	18	–	37	–	–	8	–
	Anterior leaflet	0	3	–	4	–	–	12	–

Table 1. (*Continued*)

13	Assessment:								
	UCG	3	17	41	44	15	5	25	11
	Intraoperative inspection	2	4	–	–	–	–	3	–
	Previous pulmonary artery banding	4	–	2	–	–	–	3	–
14	Surgical treatment:								
	Single patch	3	12	23	29	–	–	–	–
	Two-patch technique	2	9	20	15	–	–	–	–
15	Cleft closure:								
	Complete closure	0	3	24	32	–	1	20	6
	Partial cleft closure	4	5	15	9	–	–	0	2
	Left open	1	1	4	3	–	–	3	3
16	Associated coarctation aorta	–	3	4	–	–	–	–	–
17	Re-operation required/ outcomes	0	7	9	2	1	6	2	2
18	Overall freedom from re-operation	–	62.60%	80%	87%	85.80%	85.70%	85.70%	–
19	Follow-up:								
	Range	8 m–4 y	0.4–24.3 y	1 m–32 y	–	1–150 m	1–14 y	1–14 y	2–17 y
	Mean/Median follow-up years	–	11.2 y	8.2 y	10.3 y	60 m	4.9 y	4.9 y	9 y
20	Early mortality	0	0	3	1	0	2	1	0
21	Late Mortality/Death outcomes	0	3	0	3	1	5	1	3
22	Survival rates:								
	5 years	–	90.60%	–	93%	96.10%	91.40%	–	–
	10 years	–	90.60%	–	–	96.10%	–	–	–
	15 years	–	88.90%	84%	86%	–	–	–	–
23	Down syndrome	–	9	6	–	–	104	–	–

AVSD/AVCD = atrioventricular septal/canal defect; % = percentage; LAVV = left atrioventricular valve; DO = double orifice; m = months; MV = mitral valve; UCG = electrocardiography; y = years.

Study	Events	Sample Size	Forest plot	Proportion	95% CI
Ohta et al. 2001	5	128		3.906	1.280 to 8.880
Hoohenkerk et al. 2012	21	312		6.731	4.214 to 10.105
Pontailler et al. 2019	43	1067		4.03	2.932 to 5.390
Sharma et al. 2012	44	657		6.697	4.908 to 8.887
Pontailler/Kalfa et al. 2014	15	412		3.641	2.052 to 5.934
Ando et al. 2010	7	138		5.072	2.063 to 10.172
Lee et al.1985	25	581		4.303	2.804 to 6.287
Pooled estimate				4.883	4.173 to 5.674

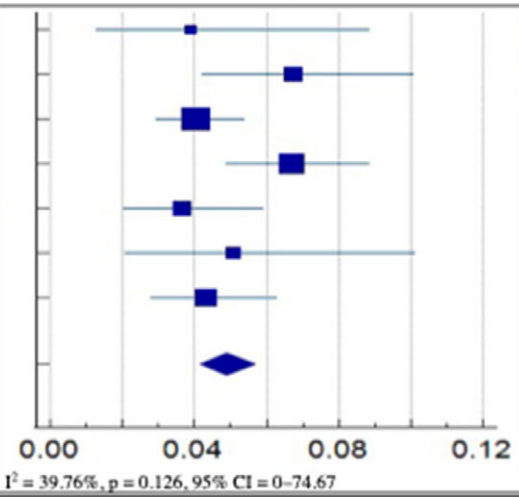

Figure 2. Forest plot showing the incidence of DOMV/DOLAVV with AVSD patients.

Study	Pre- events	Post-events	Sample Size	Forest plot	Odds ratio	95% CI
Ohta et al. 2001	3	0	5		0.0649	0.00235 to 1.794
Hoohenkerk et al. 2012	21	7	21		0.012	0.000636 to 0.227
Pontailler et al. 2019	43	8	43		0.00275	0.000153 to 0.0493
Sharma et al. 2012	35	26	44		0.371	0.144 to 0.958
Pontailler/Kalfa et al. 2014	15	0	15		0.00104	0.0000194 to 0.0558
Ando et al. 2010	7	3	7		0.0519	0.00214 to 1.254
Lee et al.1985	19	11	25		0.248	0.0739 to 0.833
Warnes et al. 1983	11	0	11		0.00189	0.0000345 to 0.104
Total (fixed effects)	154	55	171		0.0807	0.0472 to 0.138
Total (random effects)	154	55	171		0.0311	0.00618 to 0.157

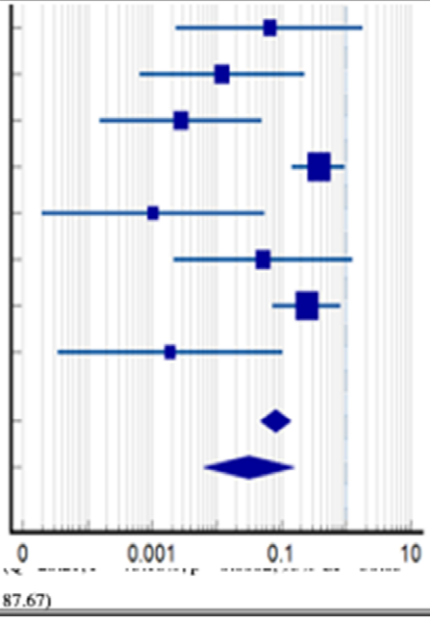

Figure 3. Forest plot showing pre-operative and post-operative regurgitation in DOMV/DOLAVV with AVSD (Odds ratio).

in moderate ($I^2 = 38.11\%$, $p = 0.126$) and severe ($I^2 = 0\%$, $p = 0.447$) status of post-operative regurgitation. The forest plots of pre-operative and post-operative regurgitation are shown in Figures 4 and 5, respectively.

Lastly, the publication biasness using Egger's test (intercept = –1.09, $p = 0.65$) and Begg's test (Kendall's Tau = 0.048, $p = 0.88$) were found to be non-significant.

Surgical interventions

Double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect patients underwent one-patch and two-patch techniques as surgical intervention based on the partial, intermediate, or complete stage of the atrioventricular septal defect condition. Out of 8 studies, only 4 studies with 117 patients provided data on surgical intervention techniques. Among 117 patients, 67 patients underwent one-patch treatment and 46 patients underwent two-patch treatment. Moreover, the clefts were partially closed in 35 patients and completely closed and sutured in 86 patients, whereas the cleft was left open in 15 patients, based on data provided by 7 studies. A significant difference in surgical intervention methods for partial and complete cleft closure was found (OR = 3.7, $p < 0.001$), as shown in Figure 6.

Further, the pooled proportions of partially and completely closed clefts associated with surgical repair of patients were 5.1% and 16.7%, respectively (Fig. 7). Furthermore, the heterogeneity

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Study	Mild	Moderate	Severe	Sample size	Mild		Moderate		Severe	
	Pre-operative regurgitation Events				Proportion	95% CI	Proportion	95% CI	Proportion	95% CI
Ohta et al. 2001	0	3	0	5	0	0.000 to 52.182	60	14.663 to 94.726	0	0.000 to 52.182
Hoohenkerk et al. 2012	7	10	4	21	33.333	14.588 to 56.968	47.619	25.713 to 70.219	19.048	5.446 to 41.907
Pontailler et al. 2019	13	12	8	43	30.233	17.182 to 46.125	27.907	15.329 to 43.669	18.605	8.391 to 33.401
Sharma et al. 2012	0	0	35	44	0	0.000 to 8.042	0	0.000 to 8.042	79.545	64.695 to 90.196
Pontailler/Kalfa et al. 2014	7	6	2	15	46.667	21.267 to 73.414	40	16.336 to 67.713	13.333	1.658 to 40.460
Ando et al. 2010	5	2	0	7	71.429	29.042 to 96.331	28.571	3.669 to 70.958	0	0.000 to 40.962
Lee et al.1985	0	17	2	25	0	0.000 to 13.719	68	46.500 to 85.050	8	0.984 to 26.031
Warnes et al. 1983	7	2	2	11	63.636	30.790 to 89.074	18.182	2.283 to 51.776	18.182	2.283 to 51.776
Pooled estimate					17.638	12.355 to 24.026	26.388	20.093 to 33.482	29.38	22.821 to 36.636

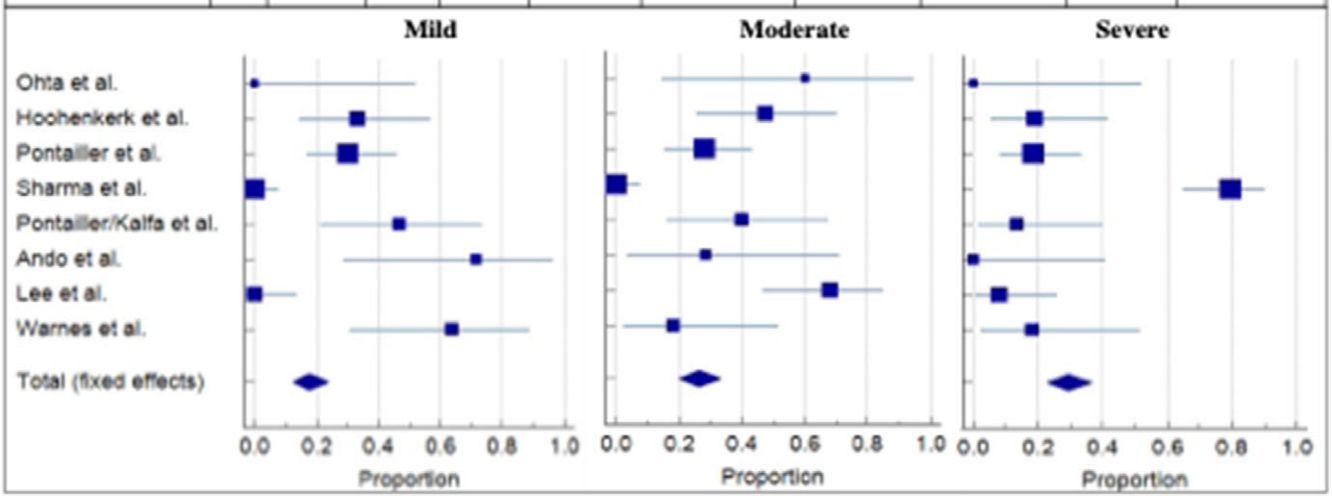

Figure 4. Forest plot showing pre-operative regurgitation in DOMV/DOLAVV with AVSD patients.

test revealed I^2 index of 83.79% for partial and 80.3% for completely closed clefts in 156 patients ($p < 0.0001$). Lastly, the publication biasness using Egger's test (intercept = 2.38, $p = 0.26$) and Begg's test (Kendall's Tau = 0.33, $p = 0.35$) were found to be non-significant.

Surgical outcomes: mortality and re-operation

Among 171 patients, the number of early and late mortality associated with surgical repair of double-orifice mitral valve/double-orifice left atrioventricular valve in atrioventricular septal defect patients were seen in 7 and 13 patients, respectively. Their estimated pooled proportions were 5% and 7.4%, respectively, as shown in Figure 8. Furthermore, heterogeneity tests on early mortality revealed insignificant and zero inconsistency ($I^2 = 0\%$, $p = 0.702$), whereas significant inconsistency was observed for late mortality ($I^2 = 53.21\%$, $p = 0.036$).

The re-operation following surgical interventions was needed in 29/171 patients only (OR = 0.042, $p < 0.001$) (Fig. 9), and the pooled estimated proportion was 16.67% along with significant inconsistency of 59.89% ($p = 0.015$). Lastly, the publication biasness using Egger's test (intercept = –2.6, $p = 0.19$) and Begg's test (Kendall's Tau = –0.29, $p = 0.32$) were found to be non-significant.

Discussion

Double-orifice mitral valve/double-orifice left atrioventricular valve is a rare congenital anomaly that is caused due to inadequate embryonic fusion of endocardial cushions and may accompany chorda-papillary anomalies including parachute mitral valve and mitral cleft.[2,5] Double-orifice mitral valve/double-orifice left atrioventricular valve substantially obstructs mitral valve inflow or produces mitral valve incompetence. Trowitzsch et al (1985) classified double-orifice mitral valve as an incomplete bridge, complete bridge, and hole type10. Eccentric or hole type is the commonest type occurs in 85% of cases and is characterised by the presence of a larger main orifice and a smaller accessory orifice either at the anterolateral or the poster medial commissure. On the other hand, central or bridge type occurs in about 15% of patients. In this, fibrous or abnormal leaflet tissue extends from the leaflet ends and divides the orifice into medial and lateral parts.[10,11] Several factors including differential patient recruitment of varied age ranges, valvular structural context aetiology, left ventricular function, and other co-morbidities have hindered the interpretation of clinical outcomes and hence, limiting the provisions for patient management.[4] A little change could affect the clinical outcomes. Based on this background, the present systematic review and meta-analysis is an attempt to pool the clinical experiences and

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Study	Mild	Moderate	Severe	Sample size	Mild		Moderate		Severe	
	Post-operative regurgitation Events				Proportion	95% CI	Proportion	95% CI	Proportion	95% CI
Ohta et al. 2001	0	0	0	5	0	0.000 to 52.182	0	0.000 to 52.182	0	0.000 to 52.182
Hoohenkerk et al. 2012	3	2	2	21	14.286	3.049 to 36.342	9.524	1.175 to 30.377	9.524	1.175 to 30.377
Pontailler et al. 2019	0	6	2	43	0	0.000 to 8.221	13.953	5.298 to 27.932	4.651	0.568 to 15.811
Sharma et al. 2012	21	0	5	44	47.727	32.461 to 63.310	0	0.000 to 8.042	11.364	3.794 to 24.558
Pontailler/Kalfa et al. 2014	0	0	0	15	0	0.000 to 21.802	0	0.000 to 21.802	0	0.000 to 21.802
Ando et al. 2010	3	0	0	7	42.857	9.899 to 81.595	0	0.000 to 40.962	0	0.000 to 40.962
Lee et al.1985	10	1	0	25	40	21.125 to 61.335	4	0.101 to 20.352	0	0.000 to 13.719
Warnes et al. 1983	0	0	0	11	0	0.000 to 28.491	0	0.000 to 28.491	0	0.000 to 28.491
Pooled estimate					16.718	11.567 to 23.006	5.143	2.403 to 9.475	5.706	2.795 to 10.183

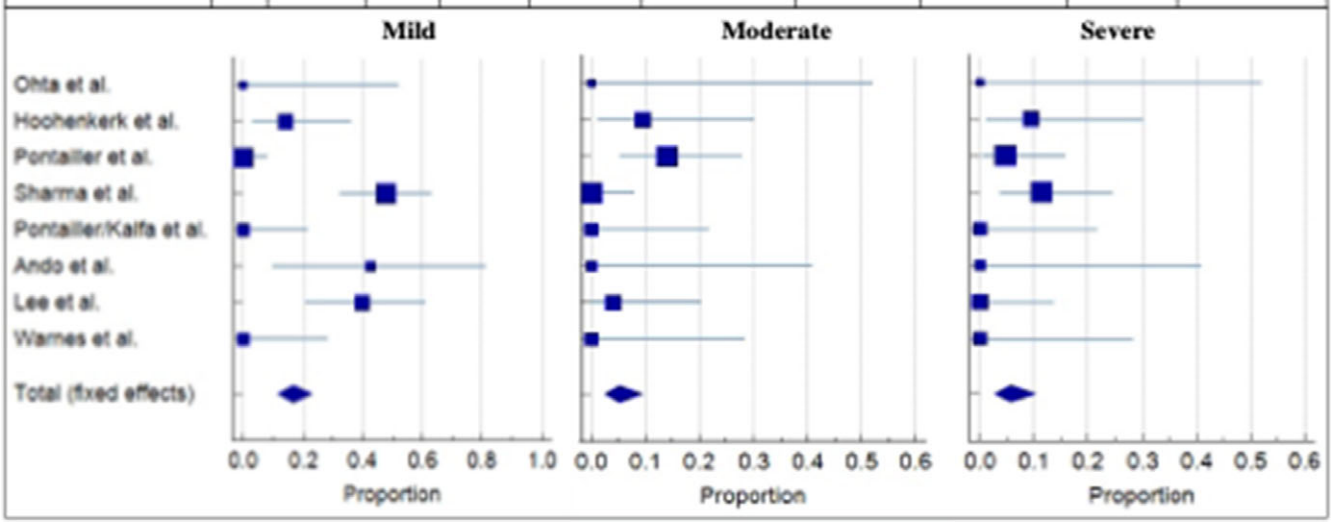

Figure 5. Forest plot showing post-operative regurgitation in DOMV/DOLAVV with AVSD patients.

surgical outcomes in atrioventricular septal defect patients who underwent repair of double-orifice mitral or left AV valves.

Double-orifice left atrioventricular valve/double-orifice mitral valve with atrioventricular septal defect has lesser incidence rates[2,8,12;] therefore, only a few series and case reports have been published in the literature. The estimated pooled proportion of incidence of double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect was 4.88%, and the heterogeneity test resulted in insignificant inconsistency (I^2) among the selected studies for meta-analysis ($p = 0.126$). The majority of the patients were infants below 3 years.[1–2,7–9,13–14] Mostly, double-orifice mitral/left AV valve in atrioventricular septal defect patients was found with a frequency of 2.1% for partial ($n = 69$), 2.1% for complete ($n = 69$), and 0.2% for intermediate type AV canal ($n = 7$). Further, the basic available information on specific outcomes of early and late mortality, regurgitation, repair techniques, and re-operation was included in the analysis.

Double-orifice mitral valve/double-orifice left atrioventricular valve with atrioventricular septal defect patients develop mitral regurgitation or stenosis,[13–14] and surgical management of such patients is quite challenging.[4] In double-orifice mitral valve, all the chordae of one papillary muscle go to one of the ostia while all of the chordae of the other papillary muscle go to the other ostia.[14] In case of extensive suturing of the cleft, stenosis may develop due to parachute mitral valve-like pathophysiology.[15] Mild regurgitation can be accepted than new significant stenosis. Treatment of non-regurgitant cleft in double-orifice mitral valve + atrioventricular septal defect is controversial because closing the cleft can create new stenosis; however, partial closure can prevent late development of mitral regurgitation. The persistent history of mitral valve regurgitation remains enigmatic. The results of post-operative regurgitation in patients showed a tremendous and significant decline in the moderate and severe status of regurgitation than in pre-operative regurgitation. Moreover, this decline in moderate ($I^2 = 38.11\%$, $p = 0.126$, 95% CI = 0–72.67) and severe ($I^2 = 0\%$, $p = 0.447$, 95% CI = 0–67.13) status of regurgitation was found to be consistent among the studies as revealed by heterogeneity test for post-operative regurgitation. Thus, the data suggest that the severity of regurgitation is corrected using the differential surgical interventions that possibly provide freedom from re-operation and better survival rates.[2,5–7,13–14]

Based on the complex aetiology of the disease, years of clinical and surgical experiences remain the key determining factor for the selection of surgical procedures. “Repair” is often opted for the

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Study	Cleft closure	Partial closure	Sample Size	Forest plot	Odds ratio	95% CI
Ohta et al. 2001	0	4	5		0.0303	0.000977 to 0.940
Hoohenkerk et al. 2012	3	5	21		0.533	0.110 to 2.594
Pontailler et al. 2019	24	15	43		2.358	0.989 to 5.624
Sharma et al. 2012	32	9	44		10.37	3.860 to 27.862
Ando et al. 2010	1	0	7		3.462	0.119 to 100.516
Lee et al.1985	20	0	25		190.091	9.920 to 3642.478
Warnes et al. 1983	6	2	11		5.4	0.777 to 37.506
Total (fixed effects)	86	35	156		3.696	2.306 to 5.924
Total (random effects)	86	35	156		3.103	0.813 to 11.835

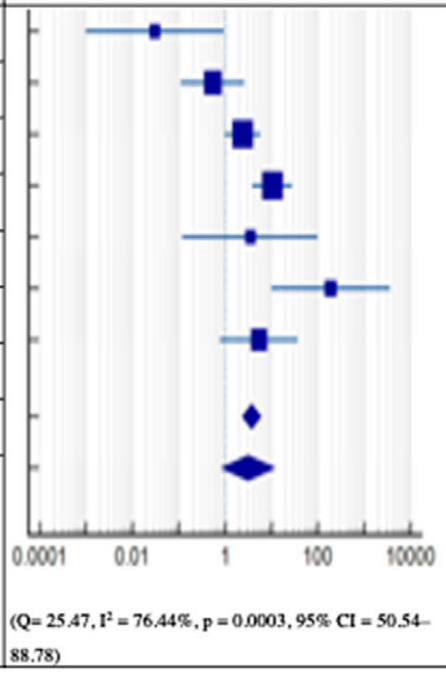

Figure 6. Forest plot showing surgical interventions in DOMV/DOLAVV with AVSD patients (Odds ratio).

Study	Events (Surgery interventions)		Sample Size	Cleft closure		Partial closure	
	Cleft closure	Partial closure		Proportion	95% CI	Proportion	95% CI
Ohta et al. 2001	0	0	5	0	0.000 to 52.182	0	0.000 to 52.182
Hoohenkerk et al. 2012	3	2	21	14.286	3.049 to 36.342	9.524	1.175 to 30.377
Pontailler et al. 2019	0	6	43	0	0.000 to 8.221	13.953	5.298 to 27.932
Sharma et al. 2012	21	0	44	47.727	32.461 to 63.310	0	0.000 to 8.042
Pontailler/Kalfa et al. 2014	0	0	15	0	0.000 to 21.802	0	0.000 to 21.802
Ando et al. 2010	3	0	7	42.857	9.899 to 81.595	0	0.000 to 40.962
Lee et al.1985	10	1	25	40	21.125 to 61.335	4	0.101 to 20.352
Warnes et al. 1983	0	0	11	0	0.000 to 28.491	0	0.000 to 28.491
Pooled estimate				16.718	11.567 to 23.006	5.143	2.403 to 9.475

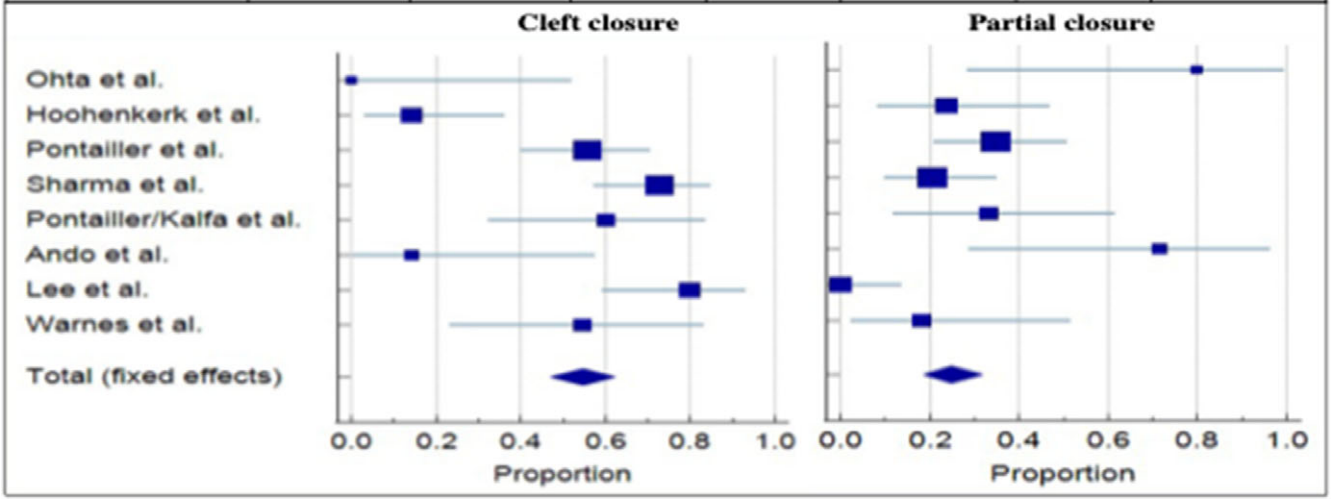

Figure 7. Forest plot showing surgical interventions in DOMV/DOLAVV with AVSD patients.

https://doi.org/10.1017/S1047951123002664 Published online by Cambridge University Press

Study	Events (Surgery interventions)		Sample Size	Early mortality		Late mortality (during follow-up)	
	Early mortality	Late mortality (during follow-up)		Proportion	95% CI	Proportion	95% CI
Ohta et al. 2001	0	0	5	0	0.000 to 52.182	0	0.000 to 52.182
Hoohenkerk et al. 2012	0	3	21	0	0.000 to 16.110	14.286	3.049 to 36.342
Pontailler et al. 2019	3	0	43	6.977	1.463 to 19.061	0	0.000 to 8.221
Sharma et al. 2012	1	3	44	2.273	0.0575 to 12.024	6.818	1.429 to 18.656
Pontailler/Kalfa et al. 2014	0	1	15	0	0.000 to 40.962	14.286	0.361 to 57.872
Ando et al. 2010	2	2	7	13.333	1.658 to 40.460	13.333	1.658 to 40.460
Lee et al.1985	1	1	25	4	0.101 to 20.352	4	0.101 to 20.352
Warnes et al. 1983	0	3	11	0	0.000 to 28.491	27.273	6.022 to 60.974
Pooled estimate				4.963	2.281 to 9.248	7.411	4.034 to 12.279

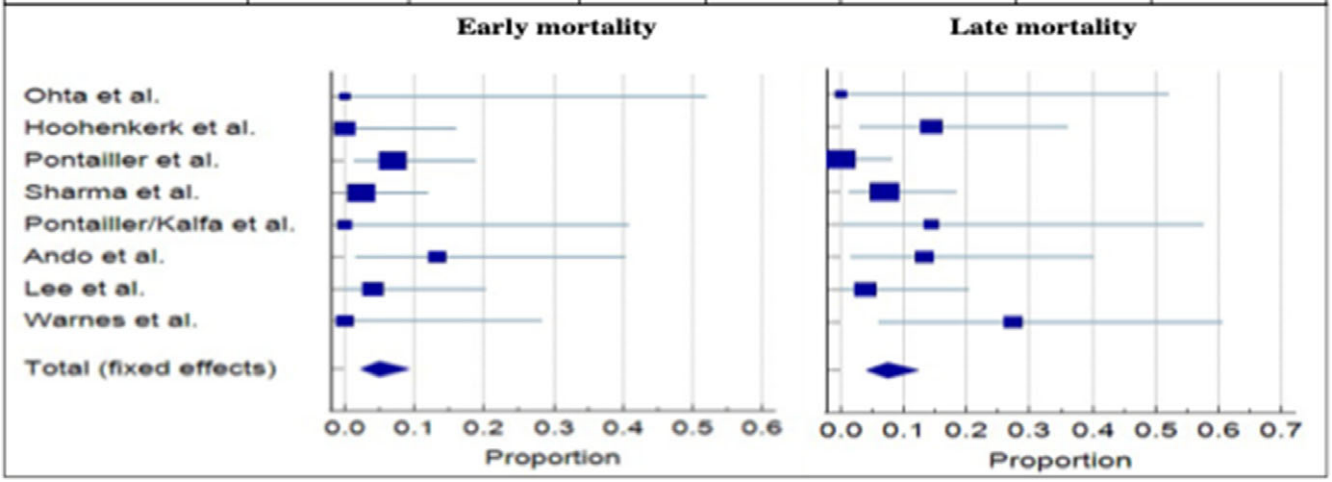

Figure 8. Forest plot showing mortality in DOMV/DOLAVV with AVSD patients.

Study	Events (Reoperation)	No events	Sample Size	Forest plot	Odds ratio	95% CI
Ohta et al. 2001	0	5	5		0.00826	0.000138 to 0.496
Hoohenkerk et al. 2012	7	14	21		0.25	0.0693 to 0.902
Pontailler et al. 2019	9	34	43		0.0701	0.0248 to 0.198
Sharma et al. 2012	2	42	44		0.00227	0.000305 to 0.0169
Pontailler/Kalfa et al. 2014	1	6	15		0.0278	0.00139 to 0.555
Ando et al. 2010	6	9	7		0.444	0.103 to 1.915
Lee et al.1985	2	23	25		0.00756	0.000980 to 0.0584
Warnes et al. 1983	2	9	11		0.0494	0.00566 to 0.431
Total (fixed effects)	29	142	171		0.0616	0.0363 to 0.104
Total (random effects)	29	142	171		0.0422	0.0118 to 0.152

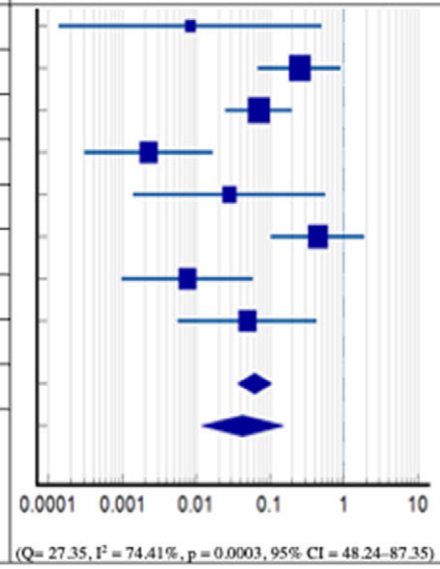

Figure 9. Forest plot showing the incidence of re-operation of DOMV/DOLAVV with AVSD patients (odds ratio).

https://doi.org/10.1017/S1047951123002664 Published online by Cambridge University Press

surgical management of regurgitation as left ventricular functions better after repair.[11] Based on the severity of lesions, the reported procedures for surgical repair varied across the studies such as single-patch vs. two-patch technique, partial vs. complete cleft closure, cleft left open, pulmonary banding, or repair of accessory orifice.[1,4,16] These variations depend on the aetiology of the disease, that is, partial, intermediate, or complete type and associated anatomic abnormalities.[11] The partial and complete cleft closure estimated the pooled proportions of 46.05% and 29.52%, respectively, and suggested partial cleft closure as a significant approach. However, the heterogeneity test revealed a high and significant inconsistency in surgical interventions of partial ($I^2 = 83.79\%$, $p < 0.0001$, 95% CI = 69.66–91.34) or completely ($I^2 = 80.3\%$, $p < 0.0001$, 95% CI = 61.88–89.82) closed clefts. The surgical interventions have shown a lot of discrepancies due to the presence of differential regurgitation (mild, moderate, and severe).[2,5–7,12–13] For instance, a completely closed cleft may create some turbulence or a parachute mitral valve with acute mitral stenosis production; or at least partial closure of a cleft should be preferred to prevent late development of mitral regurgitation.[1,16] This could affect the survival and re-operation rates. However, the ultimate aim of varied surgical procedures is to improve efficacy and minimise valvular incompetence.

The associated risk of mortality and re-operation after surgical repair of double-orifice left atrioventricular valve in atrioventricular septal defect is low. This meta-analysis showed consistency in early mortality ($I^2 = 0\%$, $p = 0.702$, 95% CI = 0–51.73); however, significant inconsistency was observed in late mortality ($I^2 = 53.21\%$, $p = 0.036$, 95% CI = 0–78.94) with heterogeneity test. Re-operation after atrioventricular septal defect repair remains a surgical challenge and the pooled estimated proportion for the incidence of re-operation following surgical interventions was only 16.67%. Despite medium proportions, significant inconsistency of 59.89% ($p = 0.015$, 95% CI: 12.70–81.57) was estimated. Studies by Ando et al., Hoohenkerk et al., and Pontailler et al. stated that re-operations for valvular regurgitation were performed within months of surgical repair.[5,7–8] Furthermore, Hoohenkerk et al. reported significantly higher overall survival at 10 and 15 years after repair and re-operation.[7] Thus, the data suggest that surgical management of double-orifice mitral or left AV valves in patients with a septal defect is considerably beneficial and provides better clinical outcomes.

Limitations

The study has several limitations. Being a rare occurring disorder, most of the publications included in the meta-analysis were relatively small in size and had the inherent biasness of retrospective studies. Another limitation is that the meta-analysis covered a very long time frame with several surgical interventions and evolving operative techniques since 1960. Nowadays, several different strategies are being explored such as percutaneous edge-to-edge techniques, coronary sinus devices, suture-based techniques, and implantation of artificial cords.[17–19] These variations caused discrepancies in quantifying the proper surgical intervention in a particular diseased condition.

Conclusion

This systematic review and meta-analysis indicate strong support for surgical repair of double-orifice mitral valve in atrioventricular septal defect patients as a significantly low trend in post-operative regurgitation was achieved. The surgical management of double-orifice mitral or AV valves is a rare, unique, and challenging task. Mitral valve repair exhibits tremendous advantages of trivial regurgitation, better survival rates, low rates of early and late mortalities, and freedom from re-operations. The outcome of the intervention depends on the aetiology of the valvular defect. The modality of surgical therapy should be more focused and detailed to reduce the current limitations of the study. More effective studies are awaited in this context of surgical repair of double-orifice mitral valve/double-orifice left atrioventricular valve that could adequately provide stronger conclusions and better future directions.

Acknowledgements. We are grateful to Dr Rajni Bala for the statistical analysis.

Competing interests. None.

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