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# Effect of posterior pericardiotomy in cardiac surgery: A systematic review and meta-analysis of randomized controlled trials

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**Background:** Posterior pericardiotomy (PP) has been shown to reduce the incidence of pericardial effusion and postoperative atrial fibrillation (POAF) after cardiac surgery. However, the procedure and the totality of its effects are poorly known in the cardiac surgery community. We performed a study-level meta-analysis of randomized controlled trials (RCTs) to evaluate the impact of PP in cardiac surgery patients.

**Methods:** A systematic literature search was conducted on three medical databases (Ovid MEDLINE, Ovid Embase, Cochrane Library) to identify RCTs reporting outcomes of patients that received a PP or no intervention after cardiac surgery. The primary outcome was the incidence of POAF. Key secondary outcomes were operative mortality, incidence of pericardial and pleural effusion, cardiac tamponade, length of stay (LOS), pulmonary complications, amount of chest drainage, need for intra-aortic balloon pump, and re-exploration for bleeding.

**Results:** Eighteen RCTs totaling 3,531 patients were included. PP was associated with a significantly lower incidence of POAF (odds ratio [OR] 0.45, 95% confidence interval [CI] 0.32–0.64, P < 0.0001), early (OR 0.18, 95% CI 0.10–0.34, P < 0.0001) and late pericardial effusion (incidence rate ratio 0.13, 95% CI 0.06–0.29, P < 0.0001), and cardiac tamponade (risk difference –0.02, 95% CI –0.04 to –0.01, P = 0.001). PP was associated with a higher incidence of pleural effusion (OR 1.42, 95% CI 1.06–1.90, P = 0.02), but not pulmonary complications (OR 0.82, 95% CI 0.56–1.19; P = 0.38). No differences in other outcomes, including operative mortality, were found.

**Conclusions:** PP is a safe and effective intervention that significantly decreases the incidence of POAF and pericardial effusion following cardiac surgery.

**Systematic review registration:** https://www.crd.york.ac.uk/prospero/ display\_record.php?RecordID=261485, identifier: CRD42021261485.

KEYWORDS

cardiac surgery, posterior pericardiotomy, postoperative atrial fibrillation, pericardial effusion, meta-analysis

# 1. Introduction

Despite advances in postsurgical management, postoperative atrial fibrillation (POAF) still represents the most frequent complication following cardiac surgery, resulting in a substantial clinical and economic burden (1–3). An important trigger of POAF, among others, seems to be the accumulation of fluid in the posterior pericardium (4, 5). Since its introduction in 1995, posterior pericardiotomy (PP) has been hypothesized to reduce the incidence of POAF and pericardial effusion by means of an incision in the posterior pericardium, allowing pericardial fluid to drain into the left pleural space (6).

Over the past two decades, multiple randomized controlled trials (RCTs) have tested this intervention, providing data on its high efficacy in reducing POAF (7–24). However, the procedure and the totality of its benefits and safety profile are poorly known in the cardiac surgery community.

We conducted a systematic review and study-level metaanalysis to evaluate the outcomes of patients that received a PP in addition to cardiac surgery compared to patients that received no additional intervention.

# 2. Methods

This review was registered with the National Institute for Health Research International Registry of Systematic Reviews (PROSPERO; CRD42021261485). The manuscript follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (25).

#### 2.1. Search strategy

A qualified librarian (MD) performed a systematic literature search to identify potential studies comparing the outcomes of patients that received cardiac surgical procedures and PP to patients that received a cardiac surgical procedure and no PP. Searched were originally run on July 2021 and updated on December 28, 2021 using the following databases (Ovid MEDLINE, Ovid EMBASE, and The Cochrane Library) from inception to present. The search strategy for Ovid MEDLINE is available in Supplementary Table 1.

## 2.2. Study selection and data extraction

After deduplication, title and abstracts of the remaining articles were screened against predefined inclusion and exclusion criteria by two authors (GS and RP-O) independently. Any discrepancies were adjudicated by the senior author (MG). All relevant English-written RCTs reporting outcomes of adult patients ( $\geq$ 18 years old) undergoing open heart surgery with and without a concomitant PP procedure were considered for inclusion. All the studies that were not RCTs were excluded. The full text of the selected manuscripts was retrieved for a second round of screening. The references were also reviewed for pertinent studies not identified through the initial search. The quality assessment of the included RCTs was performed using The Cochrane Collaboration's Risk of Bias 2 (RoB 2) tool for randomized trials (26).

The PP procedure was defined as any incision in the posterior pericardium allowing drainage of the pericardial cavity into the left pleural space, with or without the insertion of a chest tube in the posterior pericardial space. A detailed description of the steps to perform a PP has been previously published (27).

Two authors (GS and RP-O) separately performed data extraction and the accuracy was verified by the senior investigatto (MG). The following variables were extracted from each RCT: study characteristics (first author, year of publication, publishing journal, country, type of cardiac surgery, and sample size), patient demographics (age, sex, smoking status, hypertension, diabetes, and dyslipidemia), and key outcomes.

## 2.3. Outcomes

The primary outcome was the incidence of POAF. The secondary outcomes were operative mortality, early and late pericardial effusion, cardiac tamponade, pleural effusion, amount of total chest drainage (mediastinal plus pleural drainage), duration of intensive care unit (ICU) and hospital length of stay (LOS), pulmonary complications, need for intraaortic balloon pump (IABP), and re-exploration for bleeding. For the secondary outcomes, individual study definitions were used.

## 2.4. Statistical analysis

The number of events of short-term outcomes was extracted for each group and pooled with an inverse variance method and described as odds ratio (OR) with 95% confidence interval (CI). When both groups reported zero events, risk difference (RD) was used as pooled estimate.

For the only follow-up outcome (late pericardial effusion), we took into account the variability in the lengths of follow-up in each study and therefore incidence rate ratio (IRR) were pooled for this outcome. IRRis the ratio of the number of events and the number of patient-years. Inverse variance method with both fixed- and random-effect models was used to pool this estimate.

The standardized mean difference (SMD) with 95% CI was used to compare chest drainage, as well as ICU and hospital LOS between patients with and without PP.

The  $I^2$  was used to evaluate statistical heterogeneity that is the proportion of the variability in the estimates due to heterogeneity rather than by chance. A value of 25, 50, and 75% identified low, moderate and high heterogeneity, respectively. Egger's test and inspection of funnel plot was used to assess the presence of small-study effect.

A leave-one-out approach was used as sensitivity analysis for the primary outcome: the meta-analytic estimates were recalculated by excluding one study per time. Also, metaregression was performed by regressing the estimates against the preoperative characteristics (age, female sex, hypertension, dyslipidemia, smoking, and diabetes), and the type of surgery (coronary artery bypass grafting [CABG], aortic valve replacement [AVR], or other valve surgery).

In all analyses, the control group was the reference group. Statistical analyses were performed in R (version 4.2.0; R Project; R Foundation for Statistical Computing, Vienna, Austria) using the packages: meta, dmetar. A *P*-value < 0.05 was used as threshold for statistical significance.

# 3. Results

#### 3.1. Study characteristics

Of the 4,017 screened articles, 18 articles published between 1997 and 2021 met our inclusion criteria and were included in the present analysis (7–24). The PRISMA flow diagram outlining the study selection process is provided in Supplementary Figure 1.

Assessment of study quality using the RoB 2 tool showed that all but four (15, 17, 18, 21) RCTs had an unclear risk of bias regarding allocation concealment and blinding of researchers and participants. Details of the quality assessment are provided in Supplementary Table 2.

Ten (55.5%) of the included RCTs were conducted in Turkey, three (16.6%) in Iran, while China, Egypt, England, Thailand, and the United States contributed with one RCT (5.6%) each. Thirteen (72.2%) RCTs included patients undergoing isolated CABG, three (16.7%) enrolled patients undergoing either isolated CABG or CABG with valve surgery, one (5.6%) RCT enrolled patients undergoing valve and/or aortic surgery, and one (5.6%) included CABG, AVR, and aortic surgery patients. Characteristics of the included RCTs are provided in Table 1.

## 3.2. Patient characteristics

A total of 3,531 patients were pooled in the analysis. The number of patients in the included RCTs ranged from 20 to 458, with a median sample size of 146 (interquartile range: 100–209). Overall, 1,745 (49.4%) patients received a PP and 1,786 (50.6%) underwent cardiac surgery without PP.

Men represented 62.2% of the studied population (62.8 and 61.7% of the PP and control groups, respectively). The mean age range was 40.9 to 67.3 years in the PP group and 43.2 to 68.2 years in the control group. The prevalence of diabetes ranged from 17.3 to 65% in the PP group and from 10 to 56.9% in the control group. The prevalence of dyslipidemia ranged from 36 to 75% in the PP group and from 35.3 to 71.2% in the control group. The prevalence of smoking ranged from 0 to 76.1% in the PP group and from 20 to 74% in the control group. The prevalence of hypertension ranged from 20 to 80% in the PP group and from 36 to 90% in the control group.

#### 3.3. Meta-analysis

Compared to the no intervention group, patients with a PP had a significantly lower risk of POAF (OR 0.45, 95% CI 0.32–0.64, P < 0.0001; Figure 1), early pericardial effusion (OR 0.19, 95% CI 0.10–0.34, P < 0.0001; Figure 2), late pericardial effusion (IRR 0.14, 95% CI 0.07–0.30, P < 0.0001; Figure 3), and cardiac tamponade (RD -0.02, 95% CI -0.04 to -0.01, P = 0.001; Supplementary Figure 2). Patients with a PP had a higher risk of pleural effusion (265/1,165, 22.7%) compared to the no intervention group (203/1,173, 17.3%) (OR 1.42, 95% CI 1.06–1.90, P = 0.02; Supplementary Figure 3).

The leave-one-out analysis confirmed the solidity of the main analysis (Supplementary Figure 4).

No difference in operative mortality, pulmonary complications (84/1,168 [7.2%] in the PP group vs. 107/1,205 [8.9%] in the control group), need for IABP, re-exploration for bleeding, ICU LOS, hospital LOS, or chest drainage (range/mean volume in PP group: 450–1,421 ml/746 ml; range/mean volume in control group: 266–1,153 ml/696 ml) was found between groups (Supplementary Figures 5–11). A summary of all the outcomes and their reporting in each of the included RCTs are provided in Table 2 and Supplementary Table 3, respectively.

#### TABLE 1 Summary of the included RCTs.

References	Journal (2020 IF)	Country	Type of procedure	Sample size (men, %)	No of patients per arm	Outcomes and results
Arbatli et al. (7)	The Journal of Cardiovascular Surgery (1.888)	Turkey	CABG	113 (89, 79%)	PP: 54 Control: 59	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesContinuous telemetry + EKG, echocardiography, chest X-raysMain findingsNo difference in POAF between PP and control groups ( $P = 0.32$ ). Theincidence of POAF was higher in patients with mild to moderate comparedto those with no or minimal pericardial effusion ( $P = 0.017$ ). Pericardialeffusion was lower in the PP group ( $P = 0.02$ ). No significant difference inpleural effusion between groups.
Asimakopoulos et al. (8)	The Journal of Thoracic and Cardiovascular Surgery (5.209)	UK	CABG	100 (NR)	PP: 50 Control: 50	Main outcomes assessed   POAF   Assessment modalities   Continuous telemetry + EKG   Main findings   No significant difference in the incidence of AF between groups.
Bakhshandeh et al. (9)	Asian Cardiovascular and Thoracic Annals (0.49)	Iran	CABG/ Valve surgery	410 (164, 40%)	PP: 205 Control: 205	Main outcomes assessed   POAF, pericardial effusion   Assessment modalities   Not stated for POAF, echocardiography   Main findings   No significant difference in POAF between groups. At all time points, the majority of patients who underwent PP were free of effusion, but none of those in the control group were free of effusion (P < 0.05).
Cakalagaoglu et al. (10)	The Heart Surgery Forum (0.676)	Turkey	CABG/ Valve surgery	100 (83, 83%)	PP: 50 Control: 50	Main outcomes assessed   POAF, pericardial effusion   Assessment modalities   Continuous telemetry + EKG, echocardiography, chest X-ray   Main findings   No significant difference in POAF. Before discharge, the control group had a significantly higher number of patients with moderate, large, and very large pericardial effusions compared with the PP group.
Ekim et al. (11)	Medical Science Monitor (2.649)	Turkey	CABG	100 (65, 65%)	PP: 50 Control: 50	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesContinuous telemetry + EKG, echocardiography. Not stated for pleuraleffusion.Main findingsEarly pericardial effusion was significantly lower in the PP group ( $P = 0.0001$ ). The number of patients who developed POAF was significantlylower in the PP group compared with the control group ( $10 \text{ vs. } 30\%, P < 0.01$ ). No difference in the incidence of pleural effusion was found.

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References	Journal (2020 IF)	Country	Type of procedure	Sample size (men, %)	No of patients per arm	Outcomes and results
Erdil et al. (12)	Journal of Cardiac Surgery (1.62)	Turkey	Valve surgery/ Aortic	100 (39, 39%)	PP: 50 Control: 50	Main outcomes assessedPericardial effusion, pleural effusionAssessment modalitiesEchocardiography. Not stated for pleural effusion.Main findingsEarly pericardial effusion developed in 4/50 (8%) patients of the PP groupand in 19/50 (38%) of the control group ( $P < 0.001$ ). No late pericardialeffusion in the PP group, 9/50 (18%) in control group ( $P < 0.003$ ). Nosignificant difference in the incidence of pleural effusion between groups.
Farsak et al. (13)	European Journal of Cardio- Thoracic Surgery (4.191)	Turkey	CABG	150 (51, 34%)	PP: 75 Control: 75	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesContinuous telemetry + EKG, echocardiography. Not stated for pleuraleffusion.Main findingsPOAF developed in 7 patients (9.3%) in the PP group and 24 patients (32%)in the control group ( $P < 0.001$ ). Early pericardial effusion developed in42.6% (32/75) of the control group and in 10.6% (8/75) of the PP group ( $P < 0.001$ ). No late pericardial effusion developed in the PP group, while 7(9.3%) developed in the control group ( $P < 0.013$ ). No significant differencein pleural effusion.
Fawzy et al. (14)	Interactive CardioVascular and Thoracic Surgery (1.905)	Egypt	CABG	200 (132, 66%)	PP: 100 Control: 100	Main outcomes assessedPOAF, pericardial effusionAssessment modalitiesContinuous telemetry + ECG, echocardiography.Main findingsThe incidence of POAF was significantly lower in the PP group than in the control group (13 vs. 30%, $P = 0.01$ ). Postoperative pericardial effusion was significantly lower in the PP group (15 vs. 50 patients, $P = 0.04$ ).
Gaudino et al. (15)	Lancet (79.321)	USA	CABG/ AVR/ Aortic surgery	420 (318, 76%)	PP: 212 Control: 208	Main outcomes assessed   POAF, pericardial effusion, pleural effusion   Assessment modalities   Continuous telemetry and daily EKG, echocardiography, chest X-rays. CT scan in case of moderate-large pericardial effusion.   Main findings   POAF in PP group 37/212 (18%) compared to 66/208 (32%) in the no intervention group (aOR 0.44, 95% CI: 0.27–0.70; P < 0.0005). Pericardial effusion in PP 27/212 (12%) vs. 44/208 (21%) in the control group (RR 0.58, 95% CI: 0.37–0.91). No significant difference regarding pleural effusion.

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TABLE 1 (Co	ontinued)
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References	Journal (2020 IF)	Country	Type of procedure	Sample size (men, %)	No of patients per arm	Outcomes and results
Haddadzadeh et al. (16)	Acta Medica Iranica (0.26)	Iran	OPCABG	207 (142, 69%)	PP: 105 Control: 102	Main outcomes assessed   POAF, pericardial effusion   Assessment modalities   Continuous telemetry + EKG, echocardiography   Main findings   No significant difference between the two groups regarding POAF or pericardial effusion.
Kaya et al. (17)	Kardiochirurgia i Torakochirurgia Polska (0.23)	Turkey	CABG	96 (77, 80%)	PP: 30 Control: 66	Main outcomes assessedPOAF, pericardial effusionAssessment modalitiesContinuous telemetry + EKG, echocardiographyMain findingsNo significant differences were found between the groups regarding POAF $(P = 0.392)$ . The incidence of moderate to severe pericardial effusion in PPgroup was significantly lower than in the other groups on the 30thpost-operative day $(P = 0.028)$ .
Kaya et al. (18)	Interactive CardioVascular and Thoracic Surgery (1.905)	Turkey	CABG	142 (118, 83%)	PP: 70 Control: 72	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesPortable EKG telemetry, echocardiography. Not stated for pleural effusionMain findingsPOAF occurred in 27.78% of the cases in the open group and 8.57% of the patients in the closure group ( $P = 0.039$ ). Difference in pericardial effusion favored the closure group ( $P = 0.039$ ). No significant difference in pleural effusion between groups.
Kaya et al. (19)	Thoracic and Cardiovascular Surgeon (1.827)	Turkey	CABG	210 (164, 78%)	PP: 103 Control: 107	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesPortable EKG telemetry, echocardiography. Not stated for pleural effusionMain findingsStatistically significant results were obtained in the amount of PE ( $P = 0.034$ on POD 2; $P = 0.019$ on POD 5) and POAF ( $P = 0.019$ ) in favor of thestudy group. No significant difference regarding pleural effusion.
Kaygin et al. (20)	The Tohoku Journal of Experimental Medicine (1.848)	Turkey	CABG	415 (212, 51%)	PP: 213 Control: 212	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesNot stated for POAF and pleural effusion. Echocardiography.Main findingsPOAF ( $P < 0.001$ ), early ( $P < 0.001$ ) and late pericardial effusion ( $P < 0.0001$ ) occurred more frequently in the control group compared with thePP group. PP was associated with an increase in pleural effusion requiring intervention ( $P = 0.002$ ).

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TABLE 1	(Continued)
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References	Journal (2020 IF)	Country	Type of procedure	Sample size (men, %)	No of patients per arm	Outcomes and results
Kongmalai et al. (21)	Journal of the Medical Association of Thailand (0.09)	Thailand	CABG	20 (10, 50%)	PP: 10 Control: 10	Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesContinuous telemetry + EKG, echocardiography, chest X-rays.Main findingsNo significant differences in POAF ( $P = 1$ ) and early pericardial effusion ( $P = 1$ ). The incidence of pleural effusion was higher in the PP group ( $P = 0.028$ ).
Kuralay et al. (22)	The Journal of Thoracic and Cardiovascular Surgery (5.209)	Turkey	CABG 200 PP: 100 Main o (150, 75%) PP: 100 POAF, Assess Control: 100 Main o POAF, Assess Contin effusion Main o POAF, the con pericar < 0.001			Main outcomes assessedPOAF, pericardial effusion, pleural effusionAssessment modalitiesContinuous telemetry + EKG, echocardiography, Not stated for pleuraleffusion.Main findingsPOAF developed in 6 patients (6%) in PP group and in 34 patients (34%) inthe control group ( $P = 0.000007$ ). The incidence of early and latepericardial effusion was significantly more frequent in the control group ( $P$ < 0.001 for both). No statistically significant difference was found regarding
Sadeghpour et al. (23)	Multidisciplinary Cardiovascular Annals (NA)	Iran	CABG	80 (63, 79%)	PP: 40 Control: 40	Main outcomes assessed Pericardial effusion Assessment modalities Echocardiography Main findings Early pericardial effusion was more frequent in the control group (45 vs. $15\%; P = 0.01$ ). Late pericardial effusion was also more frequent in the control group (57 vs. 15%; $P = 0.01$ ).
Zhao et al. (24)	Journal of International Medical Research (1.671)	China	CABG/ Valve surgery	458 (263, 57%)	PP: 228 Control: 230	Main outcomes assessed POAF, pericardial effusion, pleural effusion Assessment modalities Not stated for POAF. Echocardiography Main findings The incidence of POAF in the PP group was significantly lower compared with the control group ( $P = 0.044$ ). The incidence of small ( $P = 0.004$ ) and moderate-to-large ( $P = 0.02$ ) pericardial effusion in the PP group was significantly lower than in the control group. The incidence of moderate-to-large pleural effusion in the PP group was significantly higher than in the control group ( $P = 0.015$ ).

aOR, adjusted odds ratio; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CT, computerized tomography; EKG, electrocardiography; IF, impact factor; NA, not available; NR, not reported; OPCABG, off-pump coronary artery bypass grafting; PO, postoperative day; POAF, postoperative atrial fibrillation; PP, posterior pericardiotomy; RCT, randomized controlled trial; SD, standard deviation.

	Experin	nental	C	ontrol				Weight	Weight
Study	Events	Total	Events	Total	Odds Ratio	OR	95%-CI	(common)	(random)
Asimakopoulos 1997	12	50	9	50	3	1.44	[0.55; 3.80]	3.7%	5.7%
Cakalagaoglu 2012	14	50	12	50		1.23	[0.50; 3.02]	4.3%	6.1%
Kongmalay 2015	4	10	4	10		1.00	[0.17; 5.98]	1.1%	2.7%
Bakhshandeh 2009	53	205	59	205	ş. <b></b>	0.86	[0.56; 1.33]	18.2%	8.8%
Haddadzadeh 2013	5	105	6	102		0.80	[0.24; 2.71]	2.3%	4.5%
Kaya 2014	6	30	18	66		0.67	[0.23; 1.90]	3.2%	5.3%
Arbatli 2003	7	54	12	59		0.58	[0.21; 1.61]	3.3%	5.5%
Zhao 2014	20	228	35	230		0.54	[0.30; 0.96]	10.1%	8.0%
Gaudino 2021	37	212	66	208		0.45	[0.29; 0.72]	16.3%	8.7%
Kaya 2016	15	103	30	107	<b>_</b> _	0.44	[0.22; 0.87]	7.2%	7.3%
Fawzy 2015	13	100	30	100		0.35	[0.17; 0.72]	6.6%	7.1%
Ekim 2006	5	50	15	50		0.26	[0.09; 0.78]	2.8%	5.0%
Kaya 2015	6	70	20	72	<b>_</b>	0.24	[0.09; 0.65]	3.6%	5.6%
Farsak 2002	7	75	24	75		0.22	[0.09; 0.55]	4.1%	6.0%
Kaygin 2011	14	213	62	212	_ <b></b> į	0.17	[0.09; 0.32]	9.0%	7.7%
Kuralay 1999	6	100	34	100		0.12	[0.05; 0.31]	4.0%	5.9%
Common effect model		1655		1696	<b>Å</b>	0.47	[0.39; 0.56]	100.0%	
Random effects model $I^2 = 66\%$ , $p < 0.01$						0.45	[0.32; 0.64]		100.0%
					0.1 0.5 1 2 10				
					PP Control POAF				

FIGURE 1

Forest plot for postoperative atrial fibrillation. CI, confidence interval; OR, odds ratio; POAF, postoperative atrial fibrillation; PP, posterior pericardiotomy.

	Experim	nental	C	ontrol				Weight	Weight
Study	Events	Total	Events	Total	Odds Ratio	OR	95%-CI	(common)	(random
Kongmalay 2015	7	10	6	10	÷	1.56	[0.24; 9.91]	1.4%	4.6%
Kaya 2016	19	103	24	107	:- <b></b> -	0.78	[0.40; 1.53]	10.8%	7.3%
Haddadzadeh 2013	11	105	14	102		0.74	[0.32; 1.71]	7.0%	7.0%
Gaudino 2021	26	212	45	208	<b>—</b>	0.51	[0.30; 0.86]	17.8%	7.6%
Kaya 2015	21	70	34	72		0.48	[0.24; 0.95]	10.4%	7.3%
Arbatli 2003	14	54	28	59		0.39	[0.18; 0.86]	7.8%	7.1%
Ekim 2006	6	50	21	50		0.19	[0.07; 0.52]	4.7%	6.6%
Kaygin 2011	10	213	46	212		0.18	[0.09; 0.36]	9.7%	7.3%
Farsak 2002	8	75	32	75	- <b></b> -	0.16	[0.07; 0.38]	6.6%	6.9%
Fawzy 2015	15	100	53	100	<b>#</b>	0.16	[0.08; 0.31]	10.8%	7.3%
Erdil 2005	4	50	19	50		0.14	[0.04; 0.46]	3.6%	6.2%
Zhao 2014	4	228	27	230		0.13	[0.05; 0.39]	4.3%	6.5%
Kaya 2014	0	30	7	66		0.13	[0.01; 2.35]	0.6%	2.8%
Sadeghpour 2011	2	40	23	40		0.04	[0.01; 0.18]	2.0%	5.3%
Kuralay 1999	1	100	54	100		0.01	[0.00; 0.06]	1.2%	4.3%
Cakalagaoglu 2012	0	50	30	50		0.01	[0.00; 0.11]	0.6%	2.9%
Bakhshandeh 2009	0	205	67	205		0.00	[0.00; 0.08]	0.6%	3.0%
Common effect model		1695		1736	0	0.29	[0.23; 0.36]	100.0%	
Random effects model					<b></b>	0.19	[0.10; 0.34]		100.0%
$I^2 = 76\%, p < 0.01$					0.001 0.1 1 10 100	0			
					PP Control				
					Early pericardial effusion				

Study	Incidence Rate Ratio	IRR	95%-CI	Weight (common)	Weight (random)
Arbatli 2003		1.09	[0.02; 54.11]	1.6%	3.2%
Kongmalay 2015			[0.02; 45.63]	1.6%	3.3%
Kaya 2015		0.64	[0.22; 1.87]	20.8%	14.5%
Kaya 2016		0.40	[0.18; 0.93]	34.5%	16.4%
Kaya 2014		0.17	[0.01; 2.91]	2.9%	5.3%
Ekim 2006		0.14	[0.01; 2.69]	2.8%	5.0%
Cakalagaoglu 2012		0.11	[0.01; 2.01]	2.8%	5.1%
Gaudino 2021		0.09	[0.00; 1.60]	2.8%	5.2%
Farsak 2002		0.07	[0.00; 1.15]	2.9%	5.3%
Kaygin 2011		0.06	[0.02; 0.26]	11.9%	11.9%
Erdil 2005	<b>_</b>	0.05	[0.00; 0.88]	3.0%	5.3%
Sadeghpour 2011		0.05	[0.01; 0.35]	6.2%	8.6%
Kuralay 1999		0.02	[0.00; 0.38]	3.1%	5.4%
Bakhshandeh 2009		0.01	[0.00; 0.22]	3.1%	5.4%
Common effect model Random effects model $I^2 = 39\%$ , $p = 0.07$			[0.13; 0.34] [0.07; 0.30]	100.0%	100.0%
	.001 0.1 1 10 PP Control Late pericardial effus	1000 sion			
FIGURE 3 Forest plot for late pericardial effusi	on. Cl, confidence interval; IRR, inciden	ce rate ratio; PP,	posterior pericardic	otomy.	

Outcome	No. of studies	Events	Patients	Effect estimate (95% CI), P-value	Heterogeneity (I <sup>2</sup> , <i>P</i> -value)
POAF	16	660	3,351	OR = 0.45 (0.32–0.64), <i>P</i> < 0.0001	65.8%, <i>P</i> < 0.001
Operative mortality	11	33	2,123	RD = -0.002 (-0.01  to  0.01), P = 0.66	0.0%, P = 0.99
Early pericardial effusion	17	678	3,431	OR = 0.19 (0.10-0.34), <i>P</i> < 0.0001	76.3%, <i>P</i> < 0.001
Late pericardial effusion	14	-	2,566	IRR = 0.14 (0.07–0.30), <i>P</i> < 0.0001	38.5%, <i>P</i> = 0.07
Chest drainage	14	-	2,019	SMD = $0.10 (-0.13 \text{ to } 0.34), P = 0.4$	86.3%, <i>P</i> < 0.001
Cardiac tamponade	15	62	3,144	RD = -0.02 (-0.04  to  -0.01), P = 0.001	55.5%, <i>P</i> = 0.01
Pleural effusion	11	468	2,338	OR = 1.42 (1.06-1.90), P = 0.02	38.4%, <i>P</i> = 0.09
Hospital LOS*	10	-	1,641	SMD = $-0.11 (-0.29 \text{ to } 0.06), P = 0.21$	60.7%, <i>P</i> = 0.01
ICU LOS*	6	-	1,243	SMD = 0.06 (-0.15  to  0.27), P = 0.57	62.9%, <i>P</i> = 0.02
Pulmonary complications	12	191	2,373	OR = 0.82 (0.56 - 1.19), P = 0.30	7.1%, P = 0.38
Need for IABP	9	105	2,096	RD = 0.003 (-0.01  to  0.02), P = 0.62	0.0%, <i>P</i> = 0.97
Re-exploration for bleeding	14	100	2,944	OR = 0.78 (0.52 to 1.19), P = 0.25	0.0%, <i>P</i> = 0.93

\*Measured in days. CI, Confidence interval; IABP, intra-aortic balloon pump; ICU, intensive care unit; IRR, incidence rate ratio; LOS, length of stay; OR, odds ratio; POAF, postoperative atrial fibrillation; RD, risk difference; SMD, standardized mean difference.

TABLE 3	Results o	f meta-regression	for the primary outcome.
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Variables	Beta $\pm$ SE, <i>P</i> -value
Age	$0.0675 \pm 0.0486, P = 0.17$
Female sex	$-0.0039 \pm 0.0116, P = 0.74$
Diabetes	$-0.0105 \pm 0.0120, P = 0.39$
Dyslipidemia	$0.0146 \pm 0.0474, P = 0.76$
Smoking	$-0.0178 \pm 0.0157, P = 0.26$
Hypertension	$0.0141 \pm 0.0133, P = 0.29$
CABG	$-0.0099 \pm 0.0102, P = 0.33$
Valve surgery	$0.0125 \pm 0.0084, P = 0.14$
Aortic valve replacement	$0.0001 \pm 0.0153, P = 0.99$

CABG, coronary artery bypass grafting; SE, standard error.

No evidence of publication bias was observed based on the Egger's intercept test (P = 0.75) (Supplementary Figure 12).

#### 3.4. Meta-regression

Meta-regression failed to identify any significant association between the tested variables and the OR for the POAF (Table 3).

# 4. Discussion

This meta-analysis of 18 studies found that patients with PP had a significantly lower incidence of POAF, early and late pericardial effusion, and cardiac tamponade; there was a significantly higher incidence of pleural effusion, but not an increased risk of pulmonary complications. No other differences in outcomes were found.

POAF is the most frequent complication following cardiac surgery, occurring in approximately one third of the patients (1, 28). POAF has been associated with extended postoperative LOS and increased hospital costs (28), as well as with major adverse postoperative outcomes including renal and heart failure, stroke, and mortality (4, 28, 29). Despite many attempts with medical therapy to prevent POAF, its incidence remains high (30). PP provides a safe and virtually zero-cost surgical alternative for the prevention of POAF. Notably, there has been only one report of complications related to PP (graft herniation) (31), and no there are no reports on damage to the phrenic nerve or the esophagus during PP. None of the studies included in this meta-analysis reported phrenic nerve or esophageal injuries.

Since the procedure was first described by Mulay et al. (6), several RCTs have tried to shed light on the relationship between PP and POAF (7–11, 13–22, 24, 32). However, most of these studies were limited in methodological quality and inadequately powered to yield statistically significant results. This prompted our group to perform the first high-quality, adequately powered RCT on the effect of posterior pericardiotomy on POAF, the Posterior Left Pericardiotomy for the prevention of AtriaL Fibrillation after Cardiac Surgery (PALACS) trial (15), which included 420 cardiac surgery patients undergoing CABG, AVR, and/or aortic surgery, notably excluding mitral and tricuspid surgeries.

In the PALACS trial, we found a significantly lower incidence of POAF among patients randomized to PP (17 vs. 32%, P = 0.0007), and a lower incidence of postoperative pericardial effusion in the PP group (12 vs. 21%, relative risk 0.58, 95% CI 0.37–0.91), but no difference in the incidence of cardiac tamponade or pleural effusion was found. In this metaanalysis, both outcomes reached statistical significance, with the incidence of cardiac tamponade being lower in the PP group and the incidence of pleural effusion being higher in PP patients. An important finding of the present analysis is that despite the higher incidence of pleural effusion, patients with PP did not have an increased risk of pulmonary complications.

This study has the following limitations. Although our systematic review identified the best available evidence evaluating the impact of PP on postoperative outcomes, the present study cannot control for individual biases of the included studies. Additionally, there was variability in POAF detection methods, perioperative management, PP technique, and in the definition and reporting of outcomes of interest. More importantly, clinical outcomes of relevance to POAF like stroke and transient ischemic attack (TIA) were not reported in most studies (88.9%) and could not be pooled for analysis.

To conclude, our meta-analysis of 18 studies found that PP is associated with a lower incidence of POAF, pericardial effusion, and cardiac tamponade, but increased incidence of pleural effusion.

# Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

## Author contributions

GS, MG, and TS : concept and design. GS and MD: systematic search. GS and RP-O: drafting the article. MR, AD, and MG: statistics. GS, RP-O, BB, MY, and DS: data collection. All authors analyzed the data interpretation, critical revision of the article, and approval of the article.

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# **Conflict of interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/ fcvm.2022.1090102/full#supplementary-material

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