Posterior left pericardiotomy for the prevention of atrial fibrillation after cardiac surgery: an adaptive, single-centre, single-blind, randomised, controlled trial

*Mario Gaudino, Tommaso Sanna, Karla V Ballman, N Bryce Robinson, Irbaz Hameed, Katia Audisio, Mohamed Rahouma, Antonino Di Franco, Giovanni J Soletti, Christopher Lau, Lisa Q Rong, Massimo Massetti, Marc Gillinov, Niv Ad, Pierre Voisine, J Michael DiMaio, Joanna Chikwe, Stephen E Fremes, Filippo Crea, John D Puskas, Leonard Girardi, for The PALACS Investigators**

Summary

Background Atrial fibrillation is the most common complication after cardiac surgery and is associated with extended in-hospital stay and increased adverse outcomes, including death and stroke. Pericardial effusion is common after cardiac surgery and can trigger atrial fibrillation. We tested the hypothesis that posterior left pericardiotomy, a surgical manoeuvre that drains the pericardial space into the left pleural cavity, might reduce the incidence of atrial fibrillation after cardiac surgery.

Methods In this adaptive, randomised, controlled trial, we recruited adult patients (aged ≥18 years) undergoing elective interventions on the coronary arteries, aortic valve, or ascending aorta, or a combination of these, performed by members of the Department of Cardiothoracic Surgery from Weill Cornell Medicine at the New York Presbyterian Hospital in New York, NY, USA. Patients were eligible if they had no history of atrial fibrillation or other arrhythmias or contraindications to the experimental intervention. Eligible patients were randomly assigned (1:1), stratified by CHA_2DS_2-VASc score and using a mixed-block randomisation approach (block sizes of 4, 6, and 8), to posterior left pericardiotomy or no intervention. Patients and assessors were blinded to treatment assignment. Patients were followed up until 30 days after hospital discharge. The primary outcome was the incidence of atrial fibrillation during postoperative in-hospital stay, which was assessed in the intention-to-treat (ITT) population. Safety was assessed in the as-treated population. This study is registered with ClinicalTrials.gov, NCT02875405, and is now complete.

Findings Between Sept 18, 2017, and Aug 2, 2021, 3601 patients were screened and 420 were included and randomly assigned to the posterior left pericardiotomy group (n=212) or the no intervention group (n=208; ITT population). The median age was 61·0 years (IQR 53·0–70·0), 102 (24%) patients were female, and 318 (76%) were male, with a median CHA_2DS_2-VASc score of 2·0 (IQR 1·0–3·0). The two groups were balanced with respect to clinical and surgical characteristics. No patients were lost to follow-up and data completeness was 100%. Three patients in the posterior left pericardiotomy group did not receive the intervention. In the ITT population, the incidence of postoperative atrial fibrillation was significantly lower in the posterior left pericardiotomy group than in the no intervention group (37 [17%] of 212 *vs* 66 [32%] of 208 [p=0·0007]; odds ratio adjusted for the stratification variable 0·44 [95% CI 0·27–0·70; p=0·0005]). Two (1%) of 209 patients in the posterior left pericardiotomy group and one (<1%) of 211 in the no intervention group died within 30 days after hospital discharge. The incidence of postoperative pericardial effusion was lower in the posterior left pericardiotomy group than in the no intervention group (26 [12%] of 209 *vs* 45 [21%] of 211; relative risk 0·58 [95% CI 0·37–0·91]). Postoperative major adverse events occurred in six (3%) patients in the posterior left pericardiotomy group and in four (2%) in the no intervention group. No posterior left pericardiotomy related complications were seen.

Interpretation Posterior left pericardiotomy is highly effective in reducing the incidence of atrial fibrillation after surgery on the coronary arteries, aortic valve, or ascending aorta, or a combination of these without additional risk of postoperative complications.

Funding None.

Introduction

Postoperative atrial fibrillation is the most frequent type of secondary atrial fibrillation and the most frequent complication of cardiac surgery.[1] Atrial fibrillation after cardiac surgery has been associated with reduced survival, increased rates of stroke and heart failure, and substantial increases in length of stay and hospital costs.[2,3]

Postoperative pericardial effusion is common after cardiac surgery[4,5] and can trigger postoperative atrial arrhythmias.[6]

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*Investigators are listed in the appendix (pp 2–3)

Department of Cardiothoracic Surgery (Prof M Gaudino MD, N B Robinson MD, I Hameed MD, K Audisio MD, M Rahouma MD, A Di Franco MD, G J Soletti MD, C Lau MD, Prof L Girardi MD) **and Department of Anesthesiology** (L Q Rong MD), **Weill Cornell Medicine, New York, NY, USA; Department of Cardiovascular Medicine, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Italy** (Prof T Sanna MD, Prof M Massetti MD, Prof F Crea MD); **Department of Cardiovascular and Pulmonary Sciences, Catholic University of the Sacred Heart, Rome, Italy** (Prof T Sanna, Prof M Massetti, Prof F Crea); **Alliance Statistics and Data Center, Weill Medical College of Cornell University, New York, NY, USA** (K V Ballman PhD); **Department of Thoracic and Cardiovascular Surgery, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH, USA** (Prof M Gillinov MD); **Division of Cardiothoracic Surgery, Washington Adventist Hospital and University of Maryland, Tacoma Park, MD, USA** (Prof N Ad MD); **Division of Cardiac Surgery, Department of Cardiology, Institut Universitaire de Cardiologie et de Pneumologie de Québec (IUCPQ), Québec City, QC, Canada** (Prof P Voisine MD); **Department of Cardiothoracic Surgery, Baylor Scott & White The Heart Hospital, Plano, TX, USA** (Prof J M DiMaio MD); **Department of Cardiac Surgery, Smidt Heart Institute, Cedars-Sinai Medical Center,**

Los Angeles, CA, USA (Prof J Chikwe MD)**; Schulich Heart Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada** (Prof S E Fremes MD)**; Department of Cardiovascular Surgery, Mount Sinai Morningside, New York, NY, USA** (Prof J D Puskas MD)

Correspondence to: Prof Mario Gaudino, Department of Cardiothoracic Surgery, Weill Cornell Medicine, New York, 10065, NY, USA
mfg9004@med.cornell.edu

See Online for appendix

Research in context

Evidence before this study

Atrial fibrillation is the most common complication after cardiac surgery and is associated with extended duration of in-hospital stay and increased adverse outcomes, including death and stroke. Pericardial effusion is very common after cardiac surgery operations, being reported in over two-thirds of patients. Clinical and experimental data suggest that even small amounts of postoperative pericardial effusion might trigger atrial arrhythmias by inducing local inflammation and oxidative damage. Posterior left pericardiotomy is a simple surgical procedure that connects the pericardial sac with the left pleural space and drains fluids and thrombi from the pericardial cavity in the postoperative period. The rationale for our study was based on a systematic review and meta-analysis of ten randomised trials including 1648 patients (822 in the posterior left pericardiotomy group and 826 in the control group) that reported a significant reduction in the risk of postoperative atrial fibrillation in the group that received posterior left pericardiotomy. However, the methodological quality of the pooled studies was low and there was considerable heterogeneity in inclusion criteria, outcome definitions, control group, and assessment methods. Because of the unconvincing evidence, the technique—although promising—is not routinely used during cardiac surgery operations.

Added value of this study

We found, in an adequately powered and rigorous prospective randomised trial, that posterior left pericardiotomy is associated with a large and significant reduction in the incidence of postoperative atrial fibrillation in patients undergoing coronary bypass, aortic valve, or aortic surgery. We found no added risk or side-effects compared with no intervention.

Implications of all the available evidence

Based on the concordance between the previous evidence and our results, the large treatment effect, and the very favourable risk to benefit ratio of the intervention, posterior left pericardiotomy should be considered during most cardiac surgery operations. However, a large pragmatic confirmatory multicentre trial including the entire spectrum of cardiac surgery operations is needed to quantify the potential clinical benefits of the intervention.

Left pericardiotomy is a simple surgical procedure in which the pericardial space is drained into the left pleural cavity through a posterior pericardial incision, and this procedure has been hypothesised to potentially reduce the incidence of postoperative atrial fibrillation.[7,8] Small studies and meta-analyses have shown a reduction in atrial fibrillation after cardiac surgery associated with posterior left pericardiotomy, but the hypothesis has not been formally tested in an adequately powered randomised trial.[9–11]

We performed a randomised trial to assess potential harms and benefits of posterior left pericardiotomy and test the hypothesis that posterior left pericardiotomy would reduce the incidence of atrial fibrillation after cardiac surgery.

Methods

Study design and participants

This randomised, adaptive, clinical trial was performed by members of the Department of Cardiothoracic Surgery from Weill Cornell Medicine (New York, NY, USA) at the New York Presbyterian Hospital in New York, NY, USA. Consecutive patients admitted to the centre were screened for inclusion, and eligible participants were adult patients (aged ≥18 years) undergoing cardiac surgery for primary, elective interventions on the coronary arteries, the aortic valve, or the ascending aorta, or a combination of these, who had no history of atrial fibrillation or other arrhythmias. Patients undergoing mitral or tricuspid valve surgery were excluded because in those patients the pathophysiology and risk of postoperative atrial fibrillation are different than in patients undergoing other cardiac surgery procedures and so might result in a heterogeneous population.[12,13] Patients with contraindications to the experimental intervention (disease of the left pleura, previous intervention in the left pleural space, or chest deformity) and those undergoing repeat operations or minimally invasive procedures were also excluded. Full eligibility criteria have been defined in the trial protocol[14] and are summarised in the appendix (p 4). All patients provided written informed consent to trial participation and data usage.

The study protocol was published a priori[14] and approved by the Weill Cornell Medicine institutional review board (approval number 1502015867). An independent data monitoring committee and an independent events adjudication committee oversaw the trial (appendix p 4).

In March, 2020, a protocol amendment was submitted and approved by the Weill Cornell Medicine Institutional Review Board to allow for clinical personnel to be involved in screening and enrolment activities because of the restriction of in-hospital access by research personnel during the height of the COVID-19 pandemic.

Randomisation and masking

Eligible patients who consented to participate in the trial were randomly assigned (1:1), to undergo either posterior left pericardiotomy or no intervention during the planned surgical procedure. To assure similar baseline risk of postoperative atrial fibrillation in the two groups, randomisation was stratified by the CHA_2DS_2-VASc score (score of ≤2 *vs* ≥3), which has been shown to predict the

risk of postoperative atrial fibrillation in patients undergoing cardiac surgery.[15,16] A computer-generated, mixed block randomisation approach, with block sizes of 4, 6, and 8, was used by one of the statisticians (MR) to generate the randomisation sequence. A treatment allocation card was electronically generated the night before the procedure and communicated to the surgical team (including MG, CL and LG) by email. Patients and assessors were blinded to treatment group assignment. Patients were to be unmasked to treatment assignment after study completion, and premature unmasking was only allowed if secondary interventions were required due to complications related to the primary intervention. Further details of randomisation and masking have been described in the trial protocol[14] and are summarised in the appendix (p 4).

Procedures

At surgery, in patients assigned to the posterior left pericardiotomy group, a 4–5 cm vertical incision posterior to the phrenic nerve and extending from the left inferior pulmonary vein to the diaphragm was performed (appendix p 8).[7] No intervention was performed in the no intervention group. Patients in both groups received routine postoperative antiarrhythmic prophylaxis with β blockers, except those who were bradycardic (heart rate <65 beats per minute), required epicardial pacing, had an atrioventricular block, or were receiving β agonists. Systemic anticoagulation was used in case of post-operative atrial fibrillation lasting more than 24 h or in case of recurrent episodes of arrhythmias. Further details about intervention and postoperative care have been described in the trial protocol[14] and are summarised in the appendix (pp 4–5).

Continuous cardiac rhythm monitoring was done using a Philips Intellivue MP70 patient monitor (Philips, Andover, MA, USA) and alarm strips during the entire postoperative in-hospital stay. Additionally, a standard 12-lead electrocardiogram (ECG) was recorded on a daily basis and collected for analysis, and additional ECGs could be ordered by the treating physician.

Clinical follow-up assessment was done via interview either in person or by telephone within 30 days after hospital discharge. Adverse events were recorded by physicians at follow-up visits and monitored throughout the study by the data monitoring committee. Adverse events were recorded by physicians during the follow-up visits and categorised using Common Terminology Criteria for Adverse Events (version 5.0).

Outcomes

The primary outcome was the occurrence of in-hospital postoperative atrial fibrillation assessed by continuous cardiac rhythm monitoring or standard 12-lead ECG during the entire postoperative in-hospital stay. Postoperative atrial fibrillation was defined as the occurrence of an irregular heart rhythm, without detectable P waves, lasting more than 30 s. An independent committee made of two cardiologists and a cardiac surgeon adjudicated all primary outcome data. Details of the methods used for rhythm monitoring and for event adjudication have been described in the trial protocol[14] and are summarised in the appendix (pp 5–6).

The secondary outcomes were the cumulative time spent in atrial fibrillation (defined as the time from the first evidence of atrial fibrillation to the first evidence of sinus rhythm restoration on cardiac monitoring strips or standard ECG), the need for antiarrhythmic medications to treat postoperative atrial fibrillation, the need for systemic anticoagulation due to postoperative atrial fibrillation (post hoc), the need for postoperative electrical cardioversion, hospital readmission (post hoc), and the duration of postoperative in-hospital stay. Safety outcomes were operative mortality, postoperative major adverse events (defined as all-cause mortality, stroke, and myocardial infarction), and postoperative clinical or imaging evidence of left pleural or pericardial effusion. Full outcome definitions are in the appendix (pp 5–6).

Statistical analysis

The primary hypothesis was that the rate of postoperative atrial fibrillation would be lower in the posterior left pericardiotomy group than in the no intervention group. Assuming a rate of postoperative atrial fibrillation of 30%, we estimated that a sample size of 322 participants would have provided 90% power to detect a 50% reduction of the primary outcome in the posterior left pericardiotomy group compared with the no intervention group; this large treatment effect was consistent with the existing evidence on posterior left pericardiotomy and was clinically relevant.[9,10] To account for possible protocol violations, loss to follow-up, and people withdrawing from the study, a total sample size of 350 patients (ie, 175 in each treatment group) was prespecified. Two efficacy interim analyses were pre-specified and done after enrolment of the first and second 100 consecutive patients. Sample size re-calculation at the time of the interim analyses was also prespecified. At the second interim analysis, the rate of atrial fibrillation was found to be lower than anticipated and the trial sample size was re-estimated at 420 patients (details are provided in the appendix [p 6]). There was no futility interim analysis. We used the Haybittle-Peto rule for efficacy analysis, so that a difference of at least four SDs for the first interim analysis and three SDs at the second interim analysis in the incidence of the primary outcome would justify a recommendation to the data monitoring committee of premature halting of the study. The corresponding χ^2 value is 16 ($\alpha=0\cdot001$).

We did the primary analysis according to the intention-to-treat (ITT) principle (ie, included all participants as if they were treated according to the group into which they were assigned), and we did a sensitivity analysis of the

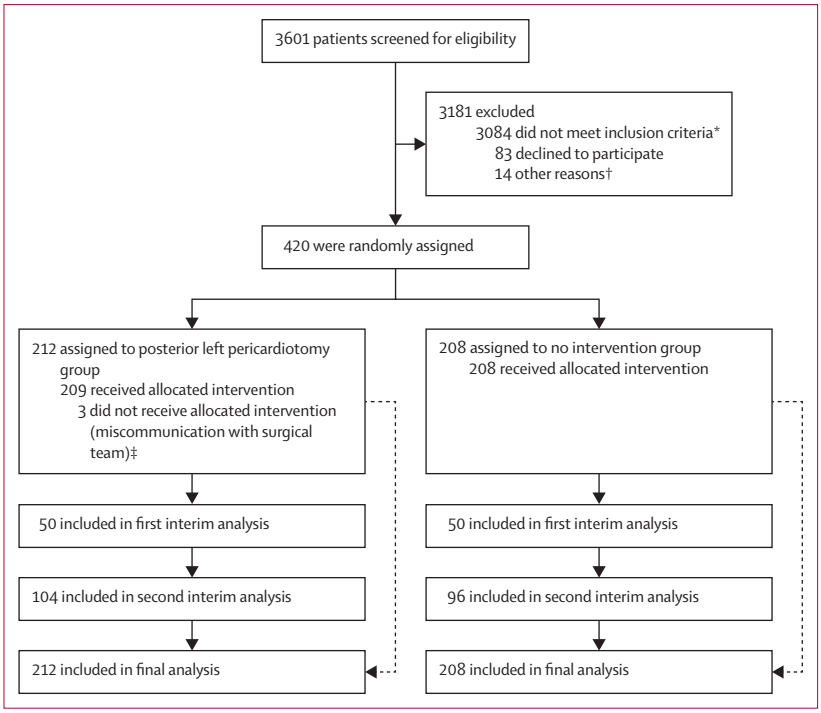

Figure 1: **Trial profile**
*2189 due to type of surgery, 447 due to rhythm abnormality, 405 due to mitral or tricuspid disease, and 43 due to chest deformity or intervention. †Other reasons were: unable to provide consent (n=12) and surgeon decision (n=2). ‡Received no intervention, and so were included in the no intervention group in the as-treated analysis.

primary outcome using the as-treated principle (ie, including all participants according to the treatment they actually received). Secondary outcomes were also analysed in the ITT population and safety outcomes in the as-treated population.

We report categorical variables as counts and proportions and continuous variables as mean (SD) or median (IQR) on the basis of normality. We assessed the differences between the posterior left pericardiotomy and the no intervention groups using the χ^2 test for categorical variables and Student's *t* test or the Mann-Whitney *U* test for continuous variables. We assessed the primary outcome using the Mantel-Haenszel test with the CHA_2DS_2-VASc stratification variable. We also assessed the primary outcome using a logistic regression model that included the stratification variable. We did a sensitivity analysis for the primary outcome using a multivariable mixed-effect logistic regression model that included the operating surgeon as a random effect and the following covariables: age, sex, diabetes status, left ventricular ejection fraction, extent of coronary disease, New York Heart Association class, chronic lung disease, EuroSCORE II, and preoperative and postoperative use of β blockers. For the primary outcome, we did prespecified subgroup and interaction-term analyses to investigate the following possible effect modifiers: age (<70 years *vs* ≥70 years), sex, left ventricular ejection fraction (<50% *vs* ≥50%), CHA_2DS_2-VASc score (≤2 *vs* ≥3), and type of surgery (ie, coronary artery bypass grafting, aortic valve procedures, or aortic procedures). Furthermore, we did an additional exploratory analysis of the primary outcome only in those who received β blockers postoperatively in the ITT population. We only analysed secondary and safety outcomes using descriptive statistics, relative risk, and risk difference.

All p values were two-sided. For the final analysis, we used an α level of 0·05 to indicate statistical significance. There was no adjustment for the minimum biases introduced by the interim analyses.

We did all statistical analyses using R (version 3.2.3). This study is registered with ClinicalTrials.gov, NCT02875405.

Role of the funding source

There was no funding source for this study.

Results

Between Sept 18, 2017, and Aug 2, 2021, 3601 patients were screened, of whom 420 underwent random assignment to the posterior left pericardiotomy group (n=212) or the no intervention group (n=208; figure 1). Enrolment was slower than expected in large part due to the COVID-19 pandemic that strongly affected New York in the first half of 2020 and led to the partial and even total suspension of elective cardiac surgery cases for most of 2020 and part of 2021.

At surgery, three (1%) patients assigned to the posterior left pericardiotomy group did not receive the assigned intervention due to miscommunication with the surgical team. The randomised allocation was followed in all patients assigned to the no intervention group. No data were missing and no patients were lost to follow-up. Hence the ITT population comprised 420 patients (212 in the posterior left pericardiotomy group and 208 in the no intervention group) and the as-treated population comprised 420 patients (209 in the posterior left pericardiotomy group and 211 in the no intervention group [including three who were not given their allocated intervention from the posterior left pericardiotomy group]).

In the ITT population, the median age was 61·0 years (IQR 53·0–70·0), 102 (24%) were women, and 318 (76%) were men. The median CHA_2DS_2-VASc score was 2·0 (IQR 1·0–3·0), and 155 (37%) patients had a CHA_2DS_2-VASc score of 3 or higher. At surgery, in the posterior left pericardiotomy group the median cross-clamp time was 81·0 min (IQR 64·0–101·0) and median operation duration was 306·0 min (IQR 262·5–366·5), and in the no intervention group the median cross-clamp time was 78·5 min (61·0–100·0) and median operation duration was 289·0 min (252·3–353·5). The two groups were balanced with respect to baseline and surgical characteristics and use of postoperative antiarrhythmic prophylaxis with β blockers (table 1).

Postoperative atrial fibrillation occurred in 37 (17%) of 212 patients in the posterior left pericardiotomy group

and in 66 (32%) of 208 patients in the no intervention group (Mantel-Haenszel p=0·0007; odds ratio adjusted for the stratification variable 0·44 [95% CI 0·27–0·70; p=0·0005]; relative risk 0·55 [95% CI 0·39–0·78]; table 2). The treatment effect was similar in all the prespecified subgroup analyses (figure 2) and in all the sensitivity analyses (appendix p 10).

The cumulative time in atrial fibrillation was 1262·2 h in the posterior left pericardiotomy group and 2277·3 h in the no intervention group (table 2). Details on the time of onset of postoperative atrial fibrillation are provided in the appendix (p 9).

The number of patients who received postoperative antiarrhythmic medication to treat postoperative atrial fibrillation and the number of patients who received systemic anticoagulation due to postoperative atrial fibrillation (post hoc) were lower in the posterior left pericardiotomy group than in the no intervention group (table 2). Eight (4%) patients in the posterior left pericardiotomy group and 15 (7%) in the no intervention group received postoperative electrical cardioversion before hospital discharge (table 2).

The median length of postoperative in-hospital stay was 5·0 days (IQR 5·0–7·0) in the posterior left pericardiotomy group and 5·0 days (5·0–7·0) in the no intervention group (table 2). The median duration of postoperative in-hospital stay was 6·0 days (IQR 5·0–8·0) for patients who had postoperative atrial fibrillation and 5·0 days (5·0–6·0) for patients who did not have postoperative atrial fibrillation.

25 (12%) of 212 patients in the posterior left pericardiotomy group and 23 (11%) of 208 in the no intervention group were readmitted to the hospital within 30 days after discharge (post hoc). Pericardial effusion was the reason for readmission in five (2%) of 208 patients in the no intervention group and no patients in the posterior left pericardiotomy group. Pleural effusion was the reason for readmission in four (2%) of 212 patients in the posterior left pericardiotomy group and in five (2%) of 208 patients in the no intervention group (appendix p 11).

In the as-treated population, two (1%) of 209 patients in the posterior left pericardiotomy group and one (<1%) of 211 in the no intervention group died within the 30 day follow-up period. Postoperative major adverse events occurred in six (3%) patients in the posterior left pericardiotomy group and in four (2%) patients in the no intervention group (table 3). No complications attributable to posterior left pericardiotomy occurred.

The number of patients with postoperative pericardial effusion was lower in the posterior left pericardiotomy group than in the no intervention group (26 [12%] of 209 *vs* 45 [21%] of 211). The number of patients with postoperative left pleural effusion was 63 (30%) of 209 in the posterior left pericardiotomy group and 67 (32%) of 211 in the no intervention group; only three

	Overall (n=420)	Posterior left pericardiotomy group (n=212)	No intervention group (n=208)
Age, years	61·0 (53·0–70·0)	61·0 (52·0–69·0)	62·0 (55·0–70·0)
Sex			
Female	102 (24%)	50 (24%)	52 (25%)
Male	318 (76%)	162 (76%)	156 (75%)
Race			
White	325 (77%)	161 (76%)	164 (79%)
Black	25 (6%)	16 (8%)	9 (4%)
Asian	18 (4%)	10 (5%)	8 (4%)
Other	52 (12%)	25 (12%)	27 (13%)
Ethnicity			
Hispanic	32 (8%)	13 (6%)	19 (9%)
Not Hispanic	388 (92%)	199 (94%)	189 (91%)
Body-mass index, kg/m²	27·7 (24·7–30·5)	27·8 (24·6–30·3)	27·5 (24·7–30·8)
Hypertension	291 (69%)	151 (71%)	140 (67%)
Diabetes	90 (21%)	45 (21%)	45 (22%)
Smoking			
Never	231 (55%)	114 (54%)	117 (56%)
Current	26 (6%)	15 (7%)	11 (5%)
Previous	163 (39%)	83 (39%)	80 (39%)
New York Heart Association class			
I–II	387 (92%)	195 (92%)	192 (92%)
III–IV	33 (8%)	17 (8%)	16 (8%)
Chronic lung disease	13 (3%)	9 (4%)	4 (2%)
Previous myocardial infarction	55 (13%)	24 (11%)	31 (15%)
Previous stroke	14 (3%)	6 (3%)	8 (4%)
Preoperative haematocrit, %	39·8 (35·8–43·2)	39·9 (35·8–43·4)	39·7 (36·0–43·1)
Left atrial size, cm	4·0 (3·6–4·1)	4·0 (3·6–4·0)	4·0 (3·7–4·1)
Left ventricular ejection fraction, %	60·0 (55·0–65·0)	60·0 (55·0–65·0)	60·0 (55·0–65·0)
CHA_2DS_2-VASc score	2·0 (1·0–3·0)	2·0 (1·0–3·0)	2·0 (1·0–3·0)
CHA_2DS_2-VASc score ≥3	155 (37%)	80 (38%)	75 (36%)
EuroSCORE II	1·40 (1·0–2·2)	1·40 (1·0–2·2)	1·30 (0·89–2·21)
Surgery type*			
Coronary artery bypass grafting	187 (45%)	95 (45%)	92 (44%)
Aortic valve procedures	223 (53%)	114 (54%)	109 (52%)
Aortic procedures	185 (44%)	102 (48%)	83 (40%)
Operating surgeon			
Surgeon 1	333 (79%)	164 (77%)	169 (81%)
Surgeon 2	48 (11%)	30 (14%)	18 (9%)
Surgeon 3	18 (4%)	10 (5%)	8 (4%)
Surgeon 4	11 (3%)	4 (2%)	7 (3%)
Surgeon 5	7 (2%)	4 (2%)	3 (1%)
Surgeon 6	2 (<1%)	0	2 (1%)
Surgeon 7	1 (<1%)	0	1 (<1%)
Cross-clamp time, min	79·0 (62·0–100·0)	81·0 (64·0–101·0)	78·5 (61·0–100·0)
Cardiopulmonary bypass time, min	103·0 (83·0–125·0)	104·0 (84·5–126·5)	100·0 (82·0–121·0)
Operation duration, min	300·0 (258·0–357·0)	306·0 (262·5–366·5)	289·0 (252·3–353·5)

Data are n (%) or median (IQR). *157 patients had more than one procedure.

Table 1: **Baseline and surgical characteristics, intention-to-treat population**

patients (1%) in the posterior left pericardiotomy group needed postoperative left pleural drainage (table 3).

Overall, 406 (97%) of 420 patients were eligible for postoperative antiarrhythmic prophylaxis with β blockers. The remaining 14 patients were not eligible because they either died intraoperatively (one patient in the posterior left pericardiotomy group) or developed postoperative atrial fibrillation before postoperative day 1 (13 patients; eight in the no intervention group and five in the posterior left pericardiotomy group). Of 406 eligible patients, 375 (92%) received β blockers: 195 (95%) of 206 in the posterior left pericardiotomy group and 180 (90%) of 200 in the no intervention group. When limiting the analysis to patients who received β blockers, postoperative atrial fibrillation occurred in 22 (11%) of 195 patients in the posterior left pericardiotomy group and in 47 (26%) of 180 patients in the no intervention group (appendix p 12).

	Overall population (n=420)	Posterior left pericardiotomy group (n=212)	No intervention group (n=208)	Relative risk (95% CI)	Risk difference (95% CI)
Primary outcome					
Postoperative atrial fibrillation	103 (25%)	37 (17%)	66 (32%)	0·55 (0·39 to 0·78)	−0·14 (−0·22 to −0·06)
Secondary outcomes					
Need for postoperative antiarrhythmic medications*	100 (24%)	36 (17%)	64 (31%)	0·55 (0·38 to 0·79)	−0·14 (−0·22 to −0·06)
Need for systemic anticoagulation (post hoc)*	42 (10%)	13 (6%)	29 (14%)	0·44 (0·24 to 0·82)	−0·08 (−0·14 to −0·02)
Need for postoperative electrical cardioversion	23 (5%)	8 (4%)	15 (7%)	0·52 (0·23 to 1·21)	−0·03 (−0·08 to 0·01)
Cumulative time in atrial fibrillation, h	3539·4	1262·2	2277·3	NA	NA
Median time in atrial fibrillation, h	24·0 (12·4 to 38·9)	23·6 (10·0 to 39·0)	24·1 (15·3 to 38·9)	0·50 (−11·36 to 8·62)	0·50 (−11·36 to 8·62)
Median duration of postoperative in-hospital stay, days	5·0 (5·0 to 7·0)	5·0 (5·0 to 7·0)	5·0 (5·0 to 7·0)	0·00 (−1·00 to 1·00)	0·00 (−1·00 to 1·00)
Median duration of total in-hospital stay, days	6·0 (5·0 to 7·0)	6·0 (5·0 to 7·0)	6·0 (5·0 to 7·0)	0·00 (−1·00 to 1·00)	0·00 (−1·00 to 1·00)
Any postoperative atrial arrhythmias	113 (27%)	45 (21%)	68 (33%)	0·65 (0·47 to 0·90)	−0·11 (−0·2 to −0·03)

Data n (%) or median (IQR), unless otherwise stated NA=not applicable. *Due to postoperative atrial fibrillation.

Table 2: **Primary and secondary outcomes, intention-to-treat population**

	n	Events (n/N %)		Log (risk ratio), 95% CI
		Left posterior pericardiotomy group	No intervention group	
Age (years)				
<70	314	17/160 (11%)	35/154 (23%)	−0·76, −1·29 to −0·23
≥70	106	20/52 (38%)	31/54 (57%)	−0·39, −0·81 to 0·02
Sex				
Male	318	31/162 (19%)	50/156 (32%)	−0·48, −0·86 to −0·10
Female	102	6/50 (12%)	16/52 (31%)	−1·03, −1·87 to −0·19
Left ventricular ejection fraction				
<50%	37	5/17 (29%)	8/20 (40%)	−0·29, −1·20 to 0·63
≥50%	366	30/187 (16%)	55/179 (31%)	−0·64, −1·03 to −0·26
CHA_2DS_2-VASc				
≤2	265	16/132 (12%)	35/133 (26%)	−0·78, −1·32 to −0·23
≥3	155	21/80 (26%)	31/75 (41%)	−0·45, −0·91 to 0·00
Type of surgery				
Coronary artery bypass grafting	187	18/95 (19%)	23/92 (25%)	−0·31, −0·84 to 0·22
Aortic valve procedure	223	21/114 (18%)	41/109 (38%)	−0·71, −1·15 to −0·26
Aortic procedure	185	17/102 (17%)	28/83 (34%)	−0·66, −1·18 to −0·14
Overall	**420**	**37/212 (17%)**	**66/208 (32%)**	**−0·59, −0·94 to −0·25**

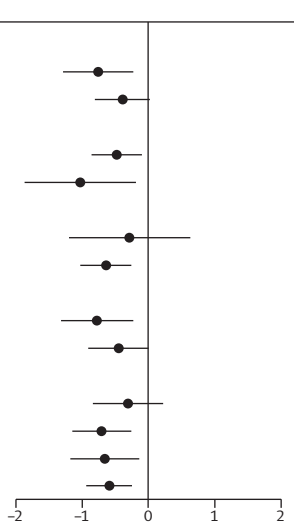

Figure 2: **Subgroup analysis for the primary outcome**
Overall risk ratio is stratified by CHA_2DS_2-VASc score.

	Overall population (n=420)	Posterior left pericardiotomy group (n=209)	No intervention group (n=211)	Relative risk (95% CI)	Risk difference (95% CI)
Operative mortality	3 (1%)	2 (1%)	1 (<1%)	2·02 (0·18 to 22·10)	0·00 (–0·02 to 0·03)
Postoperative major adverse events	10 (2%)	6 (3%)	4 (2%)	1·51 (0·43 to 5·29)	0·01 (–0·02 to 0·04)
Postoperative stroke	4 (1%)	2 (1%)	2 (1%)	1·01 (0·14 to 7·10)	0·00 (–0·03 to 0·03)
Postoperative myocardial infarction	3 (1%)	2 (1%)	1 (<1%)	2·02 (0·18 to 22·10)	0·00 (–0·02 to 0·03)
Postoperative pneumonia	11 (3%)	4 (2%)	7 (3%)	0·58 (0·17 to 1·94)	–0·01 (–0·05 to 0·02)
Surgical revision for bleeding	8 (2%)	4 (2%)	4 (2%)	1·01 (0·25 to 3·98)	0·00 (–0·03 to 0·03)
Need for postoperative intra-aortic balloon	7 (2%)	5 (2%)	2 (1%)	2·52 (0·50 to 12·86)	0·01 (–0·01 to 0·05)
Need for postoperative blood transfusion	114 (27%)	61 (29%)	53 (25%)	1·16 (0·85 to 1·59)	0·04 (–0·04 to 0·12)
Postoperative sternal complication	4 (1%)	3 (1%)	1 (<1%)	3·03 (0·32 to 28·88)	0·01 (–0·01 to 0·04)
Postoperative pericardial effusion	71 (17%)	26 (12%)	45 (21%)	0·58 (0·37 to 0·91)	–0·09 (–0·16 to –0·02)
Postoperative pericardial tamponade	2 (<1%)	1 (<1%)	1 (<1%)	1·01 (0·06 to 16·03)	0·00 (–0·02 to 0·02)
Need for postoperative pericardial drainage	2 (<1%)	1 (<1%)	1 (<1%)	1·01 (0·06 to 16·03)	0·00 (–0·02 to 0·02)
Postoperative left pleural effusion	130 (31%)	63 (30%)	67 (32%)	0·95 (0·71 to 1·26)	–0·02 (–0·10 to 0·07)
Need for postoperative left pleural drainage	3 (1%)	3 (1%)	0	NA	0·01 (–0·01 to 0·04)

Data are n (%) unless otherwise indicated. NA=not applicable.

Table 3: **Safety outcomes, as-treated population**

Discussion

In this randomised trial, posterior left pericardiotomy at the time of surgery was associated with a significant reduction in the incidence of postoperative atrial fibrillation in patients undergoing cardiac surgery operations. There were no complications attributable to posterior left pericardiotomy and the time added to the duration of surgery was minimal. The treatment effect was consistent across key clinical subgroups and with the previous evidence and our a priori estimates.

Atrial fibrillation is the most common complication after cardiac surgery, being reported in 30–40% of patients depending on the type of operation and the assessment method used.[13] Postoperative atrial fibrillation has been associated with early and late adverse events, including mortality and stroke, and extended duration of postoperative in-hospital stay and increased hospital costs.[3,17]

Small-to-moderate pericardial effusion is common after cardiac surgery operations, typically being reported in over two-thirds of patients in prospective echocardiographic studies.[4,5]

Posterior left pericardiotomy is a simple surgical procedure that connects the pericardial sac with the left pleural space and drains fluids and thrombi from the pericardial cavity in the postoperative period.[7] Previous studies have reported an association between posterior left pericardiotomy and a reduction in the incidence of postoperative atrial fibrillation, although this finding was not confirmed in all the studies.[18–20] A meta-analysis of ten small randomised trials comparing posterior left pericardiotomy with no intervention reported a significant reduction in the risk of postoperative atrial fibrillation in the group that received posterior left pericardiotomy (risk ratio 0·45 [95% CI 0·31–0·64]), but the methodological quality of the pooled studies was low to moderate and there was considerable heterogeneity in the inclusion criteria, outcome definitions, and assessment methods.[10] In our adequately powered and rigorous prospective randomised trial, we found that posterior left pericardiotomy at the time of cardiac surgery is associated with a large and significant reduction in the incidence of postoperative atrial fibrillation.

There are at least two possible mechanisms by which posterior left pericardiotomy might reduce the incidence of postoperative atrial fibrillation. Even small post-operative collection of fluid or thrombi in the pericardium, and particularly in the proximity of the atria, can trigger postoperative atrial arrhythmias, either through mechanical compression or local inflammation and oxidative stress.[6,21] Effective continuous drainage of the pericardial cavity in the postoperative period through the posterior left pericardiotomy might reduce the arrhythmic triggers and the incidence of atrial fibrillation. The incision of the pericardium in proximity of the atria might also modify the atrial geometry and haemodynamics and reduce atrial susceptibility to arrhythmic triggers, but this theory must be investigated in dedicated echocardiographic studies.

We did not observe any complication attributable to posterior left pericardiotomy and the occurrence of postoperative pleural effusion was similar in the two treatment groups. One case of herniation of a coronary bypass graft through the pericardiotomy and consequent postoperative myocardial ischaemia has been previously reported,[22] but this seems to have been an exceptional occurrence and might have been related to excessive length of the bypass conduit. To our knowledge, no complications associated with this intervention have

been reported in any of the other published studies.[10] Posterior left pericardiotomy seems to have higher efficacy, fewer side-effects, and lower costs[23] than the other interventions available to prevent postoperative atrial fibrillation (eg, prophylactic administration of β blockers, amiodarone, colchicine, steroids, magnesium, and statins, as well as postoperative overdrive atrial pacing), although formal head-to-head comparisons have not been performed.

This trial was not powered to detect a difference in the duration of postoperative in-hospital stay between treatment groups; however, postoperative in-hospital stay was longer for patients who had postoperative atrial fibrillation than for those who did not have postoperative atrial fibrillation.

Our results must be viewed considering the limitations of the trial. To avoid potential imbalances between the two treatment groups, we included patients at relatively low risk of postoperative atrial fibrillation and excluded those undergoing mitral or tricuspid valve surgery or with a history of previous atrial arrhythmias; therefore, treatment effects might be different in those patients. Also, we used continuous rhythm monitoring during the entire postoperative in-hospital stay to detect every episode of postoperative atrial fibrillation. The reported treatment effect might be lower when considering only clinically evident episodes of arrhythmia. However, most patients who had postoperative atrial fibrillation during the trial received treatment and the median duration of arrythmias was 24 h. Notably, because of the relatively small sample size, all the subgroup analyses have limited power. Another important limitation is that the trial was done at a single centre, and confirmation of our results in other institutions is necessary. Finally, the study was not powered to detect differences in clinical outcomes between the groups.

In summary, we found the performance of posterior left pericardiotomy at the time of surgery to be associated with a significant reduction in the incidence of post-operative atrial fibrillation in patients undergoing coronary, aortic valve, and aortic operations. A confirmatory multicentre trial including the entire spectrum of cardiac surgery operations is needed to quantify the potential clinical benefits of the intervention in cardiac surgery patients.

Contributors

The study design was conceived by MG, TS, FC, LG, and MM. Trial management and oversight was done by MG and LG. Patient recruitment and data collection was done by NBR, IH, KA, and GJS. Statistical analysis was done by MR and KVB vouched the results. MG and KA wrote the first draft of the manuscript. MG and LG had access to and verified the data. All authors participated in writing the final manuscript, had full access to all the data in the study, reviewed and approved the final manuscript, and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

All data requests should be submitted to the corresponding author (MG) for consideration. After publication, access to anonymised data might be granted for non-commercial research at the discretion of the corresponding author.

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