

# Effects of corticosteroids on new-onset atrial fibrillation after cardiac surgery

A meta-analysis of randomized controlled trials

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## Abstract

**Background:** Postoperative atrial fibrillation (POAF) occurs commonly after cardiac surgery. Studies suggest that corticosteroid can reduce the incident of POAF. However, the results remain controversial. This meta-analysis aimed to evaluate the efficacy and safety corticosteroid on the prevention of POAF following cardiac surgery.

**Methods:** Randomized controlled trials were identified through a systematic literature search. Two investigators independently searched articles, extracted data, and assessed the quality of included studies. Primary outcome was the incidence of POAF as well as length of hospital stay and intensive care unit stay, wound and other infection, mortality, duration of ventilation, myocardial infarction, gastrointestinal complications, high blood sugar, stroke, and postoperative bleeding.

**Results:** Fourteen studies with 13,803 patients were finally involved in the present study. Overall, corticosteroid significantly decreased the risk of POAF (relative risk [RR], 0.7; 95% confidence interval [CI], 0.55–0.89; P=.003). There were no significant differences in the incidence of length of intensive care unit stay (RR, -2.32; 95% CI, -5.44 to 0.80; P=.14) and hospital stay (RR, -0.43; 95% CI, -0.84 to -0.02; P=.04), infections (RR, 1.01; 95% CI, 0.83–1.23; P=.9), mortality (RR, 0.87; 95% CI, 0.71–1.06; P=.16), duration of ventilation (RR, -0.29; 95% CI, -0.65 to 0.07; P=.12), gastrointestinal complications (RR, 1.26; 95% CI, 0.91–1.76; P=.16), high blood sugar (RR, 1.98; 95% CI, 0.91–4.31; P=.09), stroke (RR, 0.9; 95% CI, 0.69–1.18; P=.45), postoperative bleeding (RR -44.54; 95% CI, -115.28 to 26.20; P=.22) and myocardial infarction (RR, 1.71; 95% CI, 0.96–1.43; P=.12).

**Conclusion:** Our review suggests that the efficacy of corticosteroid might be beneficial to POAF development in patients undergoing cardiac surgery. The strength of this association remains uncertain because of statistical and clinical heterogeneity among the included studies.

**Abbreviations:** CABG = coronary artery bypass grafting, CI = confidence interval, CS = corticosteroid, POAF = postoperative atrial fibrillation, RCTs = randomized controlled trials, RR = relative risk.

Keywords: atrial fibrillation, cardiac surgery, complication, corticosteroid

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# 1. Introduction

Postoperative atrial fibrillation has (POAF) been reported in 20% to 50% of patients following coronary artery bypass grafting (CABG) and is even higher after combined CABG and valve surgery.<sup>[1]</sup> New-onset atrial fibrillation after cardiac surgery also associates with numerous postoperative complications, including stroke, increased inotropic support, congestive heart failure, acute kidney injury, and death.<sup>[2,3]</sup> These in turn lead to prolonged intensive care and hospital length of stay.<sup>[3]</sup> However, the cause of POAF and its associated adverse outcomes is still not well defined.<sup>[4]</sup> Different students have illustrated that systemic inflammatory response and local inflammation of the atrium are believed to contribute to the pathogenesis of atrial fibrillation after cardiac surgery. In addition, complex inflammatory reaction may contribute to postoperative complications such as ventricular dysfunction and organ failure.<sup>[5]</sup> The relationship between inflammation and atrial fibrillation after cardiac surgery is further strengthened by studies that showed that corticosteroid (CS) prophylaxis can reduce the occurrence of atrial fibrillation after cardiac surgery. However, the potential risks of CS remain controversial and inconclusive in terms of several side effects of CS such as hyperglycemia, gastrointestinal disturbances, and postoperative infections.<sup>[6]</sup> Although previous meta-analyses of 50 small randomized controlled trials (RCTs) showed that CSs could reduce POAF when compared with placebo.<sup>[1,7]</sup> After publication of these meta-analyses, some recent reports from large RCTs of CSs in cardiac surgery showed no difference in POAF rates between the treatment group and the control group.<sup>[8,9]</sup> Taken together, use of intravenous injection steroids to prevent POAF in the cardiac surgical population still remain unclear. We performed a meta-analysis to assess determine the clinical benefits and risks of CS use in adult cardiac surgery.

## 2. Materials and methods

## 2.1. Search strategy and selection criteria

Two investigators independently searched the literatures collected in PubMed, MEDLINE, and Cochrane databases up to March 1, 2020. Search terms included: "glucocorticoid," "steroid," "hydrocortisone," "dexamethasone," "methylprednisolone," and "cardiac surgery," "cardiothoracic surgery," "heart surgery," "cardiopulmonary bypass," "CPB," "coronary artery bypass grafting," "CABG," "CAB," and clinical trial. We also sought additional studies by reviewing the reference lists of included articles, conference abstracts, and the bibliographies of expert advisors. The searches were limited to English publications in humans. This search strategy was performed iteratively until no new potential citations could be found on review of the reference lists of retrieved articles.

Studies were included if they met all of the following criteria:

- (1) RCTs about comparison of steroids with a control group;
- (2) adult patients undergoing CABG surgery (off-pump or onpump) alone or combined with valvular surgery or other cardiac surgery;
- (3) reporting outcome at least including incidence of POAF;
- (4) incidence of other postoperative complications according to our review-checklist.

Exclusion criteria included:

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- (1) not clearly define the incident of atrial fibrillation was newonset;
- (2) duplicate publication;
- (3) ongoing/unpublished study.

In addition, if the same author published multiple studies reporting outcomes at different follow-up points, we extracted patient characteristics from the first study, with data for outcomes of interest at subsequent follow-up times extracted from the later studies. When 2 studies by the same institution reported the same outcomes at similar follow-up periods, we included in our analysis either the better quality or the most informative publication. Ethical approval is unnecessary due to it is a review of previously reported articles and does not involve any processing of individual patient data.

#### 2.2. Data extraction

The qualities of each contributing evidence were evaluated following the recommended Cochrane risk of bias tool respecting to 7 parts about selection (random and allocation), performance, detection, attrition, reporting, and other bias, and each study was assessed to be of low, unclear, or high risk of bias.

All data were extracted from article texts, tables, and figures. Two individual investigators independently extracted data on patient and study characteristics, outcomes, and study quality for each trial using a standardized protocol and reporting form. Disagreements were resolved by consensus with a third reviewer.

#### 2.3. Study outcomes

The end points of this meta-analysis were as follow:

- (1) incident of POAF:
- (2) length of hospital stay;
- (3) length of intensive care unit (ICU) stay;

# Table 1

#### Characteristics of randomized controlled trials.

			I	N	Меа	an age		
Study	Year	Regimen	CS	C	CS	C	Type of surgery	Study design
Halonen et al <sup>[2]</sup>	2007	Hydrocortisone	120	127	64.4±8.4	$66.1 \pm 9.5$	On-pump CABG combined valvular surgery	RCT
Halvorsen et al <sup>[10]</sup>	2003	Dexamethasone	147	147	$63 \pm 11$	64±10	On-pump CABG	RCT
Abbaszadeh et al <sup>[11]</sup>	2012	Dexamethasone	92	92	$60.7 \pm 8.7$	59.4 <u>+</u> 10	On-pump CABG	RCT
Yared et al <sup>[12]</sup>	2007	Dexamethasone	37	34	69.2 (62,78)	74.2 (64,79)	On-pump CABG combined valvular surgery	RCT
Yared et al <sup>[13]</sup>	2000	Dexamethasone	106	110	$62.6 \pm 11.4$	63.2±11.3	On-pump CABG combined valvular surgery	RCT
Whitlock et al <sup>[14]</sup>	2006	Methylprednisolone	30	30	$67 \pm 10$	$66 \pm 11$	On-pump CABG combined valvular surgery	RCT
Suezawa et al <sup>[15]</sup>	2013	Methylprednisolone	15	15	64.8±5	$60.7 \pm 9.1$	On-pump CABG	RCT
Prasongsukarn et al <sup>[16]</sup>	2005	Methylprednisolone	43	43	67.2 (64.5-70)	61.7 (58.6-64.8)	On-pump CABG	RCT
Mirhosseini et al <sup>[17]</sup>	2011	Methylprednisolone	60	60	$63 \pm 11$	61±13	Off-pump CABG	RCT
Al-Shawabkeh et al <sup>[18]</sup>	2017	Methylprednisolone, Hydrocortisone	170	170	65.7 <u>±</u> 9.2	$64.2 \pm 8.9$	CABG orCABG+ valvular surgery	RCT
Gomez Polo et al <sup>[19]</sup>	2017	Methylprednisolone, Dexamethasone	52	52	65	63	CABG, valve replacement or combined surgery	RCT
Jacob et al <sup>[20]</sup>	2015	Dexamethasone	30	32	$70.4 \pm 9.1$	$68.9 \pm 9.0$	CABG or CABG+ valvular surgery	RCT
Dieleman et al <sup>[8]</sup>	2015	Dexamethasone	2235	2247	66.2±11.0	66.1±10.7	CABG, valvular surgery, CABG+ valvular surgery, Other cardiac surgery	RCT
Whitlock et al <sup>[9]</sup>	2015	Methylprednisolone	3755	3752	67 5±13 6	67 3±13.8	valvular surgery	RCT

CABG = coronary artery bypass grafting, CS = corticosteroid, RCTs = randomized controlled trials.



Figure 1. Risk of bias assessment. Authors' judgments about risk of bias graph for each included study (above); authors' judgments about risk of bias summary across all included studies (below).

- (4) wound infection;
- (5) other infection (urinary infect, pulmonary infection, pericarditis, mediastinitis, intravenous line infection, bacteremia, or any other infection);
- (6) mortality;
- (7) duration of;
- (8) myocardial infarction or injury;
- (9) gastrointestinal complications (upper gastrointestinal bleeding, gastrointestinal disturbance, gastritis, acute pancreatitis, perforated gastric ulcer);
- (10) high blood sugar;
- (11) stroke;
- (12) postoperative bleeding;
- (13) delirium.

# 2.4. Statistical Methods

We used fixed-effects or random-effects models to produce across-study summary relative risk (RR) with 95% confidence interval (CI). The pooled effects were calculated using fixed-effect model with the Mantel-Haenszel method when there was no significant heterogeneity or with DerSimonian-Laird weights for the random effects model when there was significant heterogeneity. The Chi-square test was used to study heterogeneity between trials, and the  $I^2$  statistic was used to estimate the percentage of total variation across studies.  $I^2$  value greater than 50% was considered as significant heterogeneity. Sensitivity analyses were performed to compare the treatment effects obtained from different subgroups with the overall treatment effects. Publication bias was explored through visual inspection of funnel plots and assessed by applying the Egger weighted regression statistic with a *P*-value < .05 indicating significant publication bias among the included studies. Correction for publication bias was performed using trim-and-fill methods. A P-value < .05 was regarded as significant. All statistical analyses were performed using Review Manager (version 5.3, Cochrane Collaboration, Oxford, UK).

# 3. Results

# 3.1. Characteristics of Included Studies

The literature search identified relative references. After selection according to the inclusion/exclusion criteria, 14 studies were eligible for meta-analysis finally.<sup>[2,8–20]</sup> A total of 13803 patients were involved, of whom 6892 patients undergoing CS group and 6911 patients undergoing control group, as summarized in Table 1. Figure 1 shows the risk of bias of the included studies. A funnel plot was generated to aid in interpretation of potential publication bias (Supplemental Figure 1, http://links.lww.com/MD/F887).

#### 3.2. POAF

A total of 13,803 patients were included from 14 RCTs, which reported data on POAF. Of these patients, 6892 cases were allocated to CS, and 6911 cases to the control group. POAF occurred in 24% in the CS group, and 26.48% in the control group. Pooled treatment effect analysis revealed that CS therapy significantly reduced the incidence of POAF (RR, 0.7; 95% CI, 0.55–0.89; P=.003; Fig. 2) using a random model. We found a moderate level of heterogeneity ( $I^2=65\%$ , P=.0003) for the pooled results for mortality.

	stero	id	Cont	lo		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H, Random, 95% Cl
Abbaszadeh 2012	32	92	19	92	7.2%	2.05 [1.06, 3.97]	-
Al-Shawabkeh 2017	36	170	65	170	9.8%	0.43 [0.27, 0.70]	
Dieleman 2012	259	784	277	781	14.6%	0.90 [0.73, 1.11]	+
Gomez Polo 2017	9	52	14	52	4.6%	0.57 [0.22, 1.46]	
Halonen 2007	44	120	62	127	9.4%	0.61 [0.36, 1.01]	
Halvorsen 2003	40	147	47	147	9.5%	0.80 [0.48, 1.31]	
Jacob 2015	9	30	12	32	3.9%	0.71 [0.25, 2.06]	
Mirhosseini 2011	10	60	13	60	4.8%	0.72 [0.29, 1.81]	
Prasongsukarn 2005	9	43	22	43	4.5%	0.25 [0.10, 0.65]	
Suezawa 2013	1	15	7	15	1.0%	0.08 [0.01, 0.79]	
Whitlock 2006	7	28	10	30	3.4%	0.67 [0.21, 2.09]	
Whitlock 2015	821	3755	846	3752	15.9%	0.96 [0.86, 1.07]	•
Yared 2000	17	106	36	110	7.3%	0.39 [0.20, 0.76]	
Yared 2007	11	37	12	34	4.2%	0.78 [0.29, 2.10]	
Total (95% CI)		5439		5445	100.0%	0.70 [0.55, 0.89]	•
Total events	1305		1442				
Heterogeneity: Tau <sup>2</sup> =	0.09; Chi <sup>2</sup>	= 37.5	1, df = 13	(P = 0.)	0003); l <sup>2</sup> =	= 65%	
Test for overall effect:	Z = 2.94 (I	P = 0.00	03)	8 - S			Favours [steroid] Favours [control]
		Figur	e 2. Fore	st plot f	for the me	ta-analysis of postoperati	ve atrial fibrillation.

# 3.3. Postoperative length of ICU and hospital stay

## 3.4. Postoperative wound and other infection

Pooled analysis revealed that CS was not associated with a reduction in length of ICU (RR, -2.32; 95% CI, -5.44 to 0.80; P = .14; Fig. 3A) and hospital stay (RR, -0.43; 95% CI, -0.84 to -0.02; P = .04; Fig. 3B) using a random effect model. Significant heterogeneity was observed among the RCTs ( $I^2 = 66\%$  and  $I^2 = 78\%$ , respectively).

A total 12 RCTs reported data on postoperative infectious complications. After removing 3 RCTs with no events in 2 arms, a total of 9219 patients from 9 studies were enrolled in the metaanalysis. In the pooled analyses, no significant difference was observed in wound complications (RR, 1.01; 95% CI, 0.83–1.23; P=.9;  $I^2=0\%$ ; Fig. 4A) and other infectious complications (RR,

	S	teroid		C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV. Random, 95% CI
Dieleman 2012	21.65	3.71	2235	22	4.45	2247	44.3%	-0.35 [-0.59, -0.11]	
Mirhosseini 2011	57.6	19.2	60	72.2	24.2	60	11.7%	-14.60 [-22.42, -6.78]	
Suezawa 2013	45.6	16.8	15	50.4	40.8	15	1.9%	-4.80 [-27.13, 17.53]	
Whitlock 2015	53.35	49.69	3755	54.35	49.69	3752	36.1%	-1.00 [-3.25, 1.25]	•
Yared 2000	36.8	28	106	47.9	113.6	110	1.9%	-11.10 [-32.99, 10.79]	
Yared 2007	34	43	37	29	13	34	4.2%	5.00 [-9.53, 19.53]	
Total (95% CI)			6208			6218	100.0%	-2.32 [-5.44, 0.80]	•
Heterogeneity: Tau <sup>2</sup> =	5.70; Ch	i <sup>2</sup> = 14.	66, df =	5 (P = (	0.01); F	2 = 66%		-	
Test for overall effect:	Z = 1.46	(P = 0.	14)		1				-50 -25 0 25 50
A									ravours [experimental] ravours [control]
		steroid	ł		Contro	I		Mean Difference	Mean Difference
Study or Subgroup	Mean	n SD	) Tota	I Mean	SD	Tota	I Weigh	t IV, Random, 95% C	I IV. Random, 95% CI
Al-Shawabkeh 2017	6.02	2 2.25	5 170	5.95	5 1.95	170	17.8%	6 0.07 [-0.38, 0.52]	+
Dieleman 2012	9.4	4 4.45	2235	5 9.7	4.45	2247	20.7%	-0.30 [-0.56, -0.04]	-
Mirhosseini 2011	5.9	9 1.2	. 60	7.4	1 2.08	60	15.19	6 -1.50 [-2.11, -0.89]	-
Suezawa 2013	14	4 7	15	5 18	3 9	15	0.5%	-4.00 [-9.77, 1.77]	
Whitlock 2006	(	6 1	30	) 6	5 2	30	12.2%	6 0.00 [-0.80, 0.80]	+
Whitlock 2015	9.1	7 4.45	3755	5 9.7	4.45	3752	2 21.5%	6 0.00 [-0.20, 0.20]	
Yared 2000	11	7 5.2	100	5 7.3	5.3	110	6.2%	-0.30 [-1.70, 1.10]	
Yared 2007	(	6 4	37	8	3 2	34	5.9%	6 -2.00 [-3.45, -0.55]	
Total (95% CI)			6408	i.		6418	100.09	6 -0.43 [-0.84, -0.02]	•
Heterogeneity: Tau <sup>2</sup>	= 0.19: 0	$Chi^2 = 3$	31.13. 0	f = 7 (F	< 0.00	001); l <sup>2</sup>	= 78%		
Tool for some li offer	+ 7 = 20	7 (D -	0.04)				1110 4040		-10 -5 0 5 10
lest for overall effec		<i>//</i> (F -	0.041						

Figure 3. Forest plot for the meta-analysis of postoperative length of ICU (A) and hospital stay (B). ICU = intensive care unit.

	stero	id	Contr	ol		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C		M-H, Rand	lom, 95% Cl	
Abbaszadeh 2012	3	92	2	92	1.1%	1.52 [0.25, 9.30]			-	
Al-Shawabkeh 2017	11	170	9	170	4.5%	1.24 [0.50, 3.07]			-	
Dieleman 2012	34	2235	32	2247	15.8%	1.07 [0.66, 1.74]			-	
Gomez Polo 2017	1	52	1	52	0.5%	1.00 [0.06, 16.43]		31		
Halonen 2007	17	78	17	71	6.4%	0.89 [0.41, 1.90]			-	
Halvorsen 2003	0	147	1	147	0.4%	0.33 [0.01, 8.19]	-			
Prasongsukarn 2005	2	43	2	43	0.9%	1.00 [0.13, 7.44]				
Whitlock 2015	151	3755	151	3752	70.4%	1.00 [0.79, 1.26]				
Total (95% CI)		6572		6574	100.0%	1.01 [0.83, 1.23]				
Total events	219		215							
Heterogeneity: Tau <sup>2</sup> = (	0.00: Chi <sup>2</sup>	= 1.02	df = 7 (P	= 0.99	): $l^2 = 0\%$				t t	
Test for overall effect: 2	Z = 0.13 (1	= 0.9	0)		,,		0.01	0.1	1 10	100
		010	-/					Favours [steroid]	Favours [control]	
0										
	stero	id	Contr	ol		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	l	M-H, Rand	om, 95% Cl	2
Abbaszadeh 2012	2	92	2	92	3.3%	1.00 [0.14, 7.25]		-		
Al-Shawabkeh 2017	3	170	2	170	3.9%	1.51 [0.25, 9.15]			-	
Dieleman 2012	212	2235	333	2247	34.9%	0.60 [0.50, 0.72]				
Gomez Polo 2017	9	52	5	52	8.2%	1.97 [0.61, 6.33]		-	-	
Halonen 2007	0	120	0	121		Not estimable				
Halvorsen 2003	3	147	1	147	2.6%	3.04 [0.31, 29.58]				
Mirhosseini 2011	1	60	5	60	2.8%	0.19 [0.02, 1.65]				
Prasongsukarn 2005	3	43	0	43	1.5%	7.52 [0.38, 150.10]		2		
Suezawa 2013	0	15	0	15		Not estimable				
Whitlock 2006	5	30	2	30	4.2%	2.80 [0.50, 15.73]				
Whitlock 2015	465	3755	493	3752	36.2%	0.93 [0.82, 1.07]				
Yared 2000	2	106	1	110	2.3%	2.10 [0.19, 23.47]		-		
Yared 2007	0	37	0	34		Not estimable				
Total (95% CI)		6862		6873	100.0%	0.94 [0.65, 1.38]		<	-	
Total events	705		844							
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2	$0.10; Chi^2$ Z = 0.29 (F	= 24.7	5, df = 9 ( 7)	P = 0.0	03); l <sup>2</sup> = 64	4%	0.01	0.1	1 10	100
В			050					Favours [sterold]	Favours [control]	



0.94; 95% CI, 0.65–1.38;  $I^2 = 64\%$  Fig. 4B) which were defined as urinary infect, pulmonary infection, pericarditis, mediastinitis, intravenous line infection, bacteremia, or any other infection.

#### 3.5. Postoperative mortality

As shown in Figure 5A, Pooled treatment effect analysis revealed that CS therapy could not reduce incidence of postoperative mortality (RR, 0.87; 95% CI, 0.71–1.06; P=.16). No heterogeneity was observed among the RCTs ( $I^2=0\%$ , P=.98)

#### 3.6. Postoperative duration of ventilation

The pooled results showed no significant difference in the duration of mechanical ventilation in hours between the treatment groups (RR, -0.29; 95% CI, -0.65 to 0.07; P=.12, Fig. 5B). We found a medium level of heterogeneity ( $I^2=46\%$ , P=.10) in the pooled results.

## 3.7. Postoperative myocardial infarction

The analysis indicated the risk of Myocardial infarction rates were not significant difference between CS group and placebo group (RR, 1.71; 95% CI, 0.96–1.43; P=.12; Fig. 5C) and found a low level heterogeneity ( $I^2=6\%$ , P=.39) in the pooled results for myocardial infarction (MI).

## 3.8. Postoperative gastrointestinal complications

The rate of gastrointestinal complications was similar in both groups (RR, 1.26; 95% CI, 0.91–1.76; P=.16; Fig. 5D). And no heterogeneity was found ( $I^2=0\%$ , P=.68) for the pooled results.

#### 3.9. Postoperative high blood sugar

CS treatment did not increase the risk of high blood sugar after cardiac surgery compared with control groups (RR, 1.98; 95% CI, 0.91–4.31; P=.09; Fig. 5E). There was no heterogeneity across the trials ( $I^2=0\%$ , P=.49).

## 3.10. Postoperative stroke

Figure 6A shows the overall RR as well as the RRs of individual trials regarding stroke. No heterogeneity across the trials was observed regarding this event ( $I^2 = 0\%$ , P = 1.00). There was no



Figure 5. Forest plot for the meta-analysis of postoperative mortality (A), duration of ventilation (B), myocardial infarction (C), gastrointestinal complications (D), and high blood sugar (E).

	stero	id	Cont	rol			Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weigh	nt M-	H. Random, 95% C	1	M-H, Rand	om, 95% Cl	
Dieleman 2012	29	2235	32	2247	28.59	10	0.91 [0.55, 1.51]		-	-	
Halonen 2007	1	120	1	121	0.99	10	1.01 [0.06, 16.31]		-		
Suezawa 2013	0	15	0	15			Not estimable				
Whitlock 2006	1	30	1	30	0.99	10	1.00 [0.06, 16.76]		-		
Whitlock 2015	71	3755	79	3752	69.6%	10	0.90 [0.65, 1.24]		-	•	
Total (95% CI)		6155		6165	100.09	10	0.90 [0.69, 1.18]		•		
Total events	102		113								
Heterogeneity: Tau <sup>2</sup>	= 0.00; Chi	<sup>2</sup> = 0.01	, df = 3 (F	P = 1.00	$);  ^2 = 0$	%		-			+
Test for overall effect	: Z = 0.75	(P = 0.4)	5)		1.00			0.02	0.1	1 10	50
A									Favours [steolo]	Favours [control]	
	steroi	d	c	Control			Mean Difference		Mean	Difference	
Study or Subgroup	Mean	SD Tota	Mean	SD	Total	Weight	IV. Random, 95	% CI	IV. Ran	dom. 95% CI	~
Abbaszadeh 2012	415 1	54 9	2 421	160	92	47.9%	-6.00 [-51.38, 39	.38]		+	
Halvorsen 2003	703 2	47 14	7 744	279	147	41.7%	-41.00 [-101.24, 19	.24]		-	
Whitlock 2006	502.14 303.	.58 3	0 738.48	467.05	30	10.4%	-236.34 [-435.67, -37	.01]			
Total (95% CI)		26	9		269	100.0%	-44.54 [-115.28, 26	.20]		•	
Heterogeneity: Tau <sup>2</sup> = 21	181.98; Chi <sup>2</sup>	= 5.26, d	f = 2 (P = 0)	0.07); l <sup>2</sup> :	= 62%		•	-	500 050		-
Test for overall effect: Z	= 1.23 (P = 0	).22)							-500 -250 Favours (steroir	di Eavours [control]	
В									T avours [storoit		
	stero	id	Contr	ol			Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	t M-H	I. Random, 95% CI		M-H, Rand	om, 95% Cl	
Dieleman 2012	205	2235	262	2247	47.6%		0.77 [0.63, 0.93]		=		
Prasongsukarn 2005	2	43	2	43	1.5%		1.00 [0.13, 7.44]				
Whitlock 2015	295	3755	289	3751	50.9%	•	1.02 [0.86, 1.21]				
Total (95% CI)		6033		6041	100.0%	5	0.89 [0.69, 1.14]			1	
Total events	502		553								
Heterogeneity: Tau <sup>2</sup> =	= 0.02; Chi <sup>2</sup>	= 4.89,	df = 2 (P	= 0.09)	; l <sup>2</sup> = 59	1%		100	01	10	50
Test for overall effect:	Z = 0.92 (	P = 0.36	5)					0.02	Eavours [storoid]	Eavours [control]	50
C									avours [sterold]	r avours [control]	

Figure 6. Forest plot for the meta-analysis of postoperative stroke (A), bleeding (B), and delirium (C).

significant difference in the risk of stroke between CS groups and control groups (RR, 0.9; 95% CI, 0.69-1.18; P=.45).

#### 3.11. Postoperative bleeding

Pooled effects showed no significant difference in blood lose after cardiac surgery (RR -44.54; 95% CI, -115.28 to 26.20; P=.22; Fig. 6B). There was significant heterogeneity among the studies ( $I^2$ =62%; P=.07).

#### 3.12. Postoperative delirium

Figure 6C shows the overall RR as well as the RRs of individual trials regarding delirium. There was a medium level of heterogeneity across the trials ( $I^2 = 59\%$ ; P = .09). The analysis indicated that there was no significant difference in the risk of delirium between CS groups and control groups (8.32% vs 9.15%; RR, 0.89; 95% CI, 0.69–1.41; P = .36).

## 3.13. Subgroup analyses of POAF

The effect of steroids on incidence of new-onset atrial fibrillation did not differ based on steroid type (Fig. 7). However, trials of low dose steroids (3 studies, 725 patients) were associated with a

smaller clinical benefit (RR=0.96; 95% CI, 0.50–1.86; P=.92;  $I^2$ =66%), whereas trials of medium dose steroids (11 studies, 10,159 patients) were associated with a greater clinical benefit (RR=0.63; 95% CI, 0.48–0.83; P=.001;  $I^2$ =76%). Trials of isolated CABG (13 studies, 1208 patients) were not associated with a benefit (RR=0.64; 95% CI, 0.29–1.41; P=.27;  $I^2$ =77%).

# 4. Discussion

Atrial fibrillation is a very common complication after cardiac surgery. Previous small RCTs and meta-analyses demonstrate that CSs could reduce the incidence of POAF when compared with placebo. However, some recent reports from large RCTs conclude that there is no protective effect of CSs on the incidence of new-onset AF after cardiac surgery.<sup>[8,9]</sup> Our meta-analysis revealed that using steroids both intraoperatively and postoperatively proved to be safe and effective in reducing the incidence of POAF without increasing the incidence of postoperative complications and adverse effects due to CS therapy.

Considering the contradictious conclusions of different RCTs, we included 5 large trials (n > 200) into subgroup analysis, which also suggesting that perioperative steroid use may decrease the incidence of atrial fibrillation after cardiac surgery. The mechanism behind the beneficial effects of steroid on the

Al-Shawabkeh 2017	Events	Total	Events	Total	Weight M-	H. Random, 95% Cl	M-H. Random. 95% Cl
I-Onawabken 2017	20	170	05	170	3 70/	0 42 10 27 0 201	
Dieleman 2012	30	794	277	791	4 7%	0.45 [0.27, 0.70]	
Halonen 2007	44	120	62	127	2 5%	0.61 [0.36 1.01]	
Whitlock 2015	821	3755	846	3752	5.4%	0.96 10.86 1.071	+
(ared 2000	17	106	36	110	1.8%	0.39 10 20, 0 761	
Subtotal (95% CI)		4935		4940	17.1%	0.69 [0.52, 0.92]	•
Total events	1177		1286				
Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z	.07; Chi <sup>2</sup> = 2.49 (F	= 18.69,	df = 4 (P	= 0.000	19); I <sup>2</sup> = 79%		
1.2.2 methylprednisold	one	-					
Mirhosseini 2011	10	60	13	60	1.1%	0.72 [0.29, 1.81]	
Prasongsukarn 2005	9	43	22	43	1.0%	0.25 [0.10, 0.65]	
Suezawa 2013	1	15	7	15	0.2%	0.08 [0.01, 0.79]	• • • • • • • • • • • • • • • • • • •
Whitlock 2006	7	28	10	30	0.8%	0.67 [0.21, 2.09]	
Whitlock 2015	821	3755	846	3752	5.4%	0.96 [0.86, 1.07]	
Subtotal (95% CI)		3901		3900	8.5%	0.54 [0.27, 1.07]	
lotal events Heterogeneity: Tau <sup>2</sup> = 0.	.35; Chi <sup>2</sup>	= 12.66,	898 df = 4 (P	= 0.01)	l <sup>2</sup> = 68%		
lest for overall effect: Z	= 1.77 (F	<sup>2</sup> = 0.08)					
.2.3 dexamethasone	-		-	-	1.004	0.05 14 00 0.07	
Abbaszadeh 2012	32	92	19	92	1.8%	2.05 [1.06, 3.97]	
Dieleman 2012	259	784	211	781	4.7%	0.90 [0.73, 1.11]	
Halvorsen 2003	40	14/	4/	14/	2.5%	0.80 [0.48, 1.31]	
(ared 2000	17	106	36	110	1.8%	0.39 [0.20, 0.76]	
(ared 2007	11	37	12	34	1.0%	0.78 [0.20, 0.76]	
Subtotal (95% CI)		1196	12	1196	12.7%	0.84 [0.58, 1.23]	+
otal events	368		403			the ferror meal	
leterogeneity: Tau <sup>2</sup> = 0.	.12; Chi2	= 12.50	df = 5 (P	= 0.031	I <sup>2</sup> = 60%		
lest for overall effect: Z	= 0.88 (F	P = 0.38)	31	5.00)	1		
.2.4 medium dose							
Al-Shawabkeh 2017	36	170	65	170	2.7%	0.43 [0.27, 0.70]	
Dieleman 2012	259	784	277	781	4.7%	0.90 [0.73. 1.11]	-+
Gomez Polo 2017	9	52	14	52	1.1%	0.57 [0.22, 1.46]	
Jacob 2015	9	30	12	32	0.9%	0.71 [0.25, 2.06]	
Mirhosseini 2011	10	60	13	60	1.1%	0.72 [0.29, 1.81]	
Prasongsukarn 2005	9	43	22	43	1.0%	0.25 [0.10, 0.65]	
Suezawa 2013	1	15	7	15	0.2%	0.08 [0.01, 0.79]	• • • • • • • • • • • • • • • • • • • •
Whitlock 2006	7	28	10	30	0.8%	0.67 [0.21, 2.09]	
Whitlock 2015	821	3755	846	3752	5.4%	0.96 [0.86, 1.07]	T
fared 2000	17	106	36	110	1.8%	0.39 [0.20, 0.76]	
fared 2007	11	37	12	34	1.0%	0.78 [0.29, 2.10]	
Subtotal (95% CI)		5080		5079	20.6%	0.63 [0.48, 0.83]	
Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z	.09; Chi <sup>2</sup> = 3.26 (F	= 29.05, P = 0.001	df = 10 ( )	P = 0.00	11); I <sup>z</sup> = 66%		
1.2.5 low dose Abbaszadeb 2012	32	92	19	92	1.8%	2 05 [1 06 3 97]	
Halonen 2007	44	120	62	127	2.5%	0.61 [0.36, 1.01]	
Halvorsen 2003	40	147	47	147	2.5%	0.80 [0.48, 1.31]	
Subtotal (95% CI)		359		366	6.8%	0.96 [0.50, 1.86]	-
Total events	116		128				
Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z	.26; Chi <sup>2</sup> = 0.11 (F	= 8.46, d = 0.92)	f = 2 (P =	= 0.01);	<sup>2</sup> = 76%		
1.2.6 isolated CABG				92	1 8%	2 05 [1 06, 3.97]	
1.2.6 isolated CABG	32	92	10				10 10 10 10 10 10 10 10 10 10 10 10 10 1
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003	32 40	92 147	19 47	147	2.5%	0.80 [0.48, 1.31]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Mirhosseini 2011	32 40 10	92 147 60	19 47 13	147 60	2.5%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Mirhosseini 2011 Prasongsukarn 2005	32 40 10 9	92 147 60 43	19 47 13 22	147 60 43	2.5% 1.1% 1.0%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Mirhosseini 2011 Prasongsukarn 2005 Suezawa 2013	32 40 10 9	92 147 60 43 15	19 47 13 22 7	147 60 43 15	2.5% 1.1% 1.0% 0.2%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Mirhosseini 2011 Prasongsukarn 2005 Suezawa 2013 Subtotal (95% CI)	32 40 10 9 1	92 147 60 43 15 357	19 47 13 22 7	147 60 43 15 357	2.5% 1.1% 1.0% 0.2% 6.7%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Wirhosseini 2011 Prasongsukarn 2005 Suezawa 2013 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0	32 40 10 9 1 92 58: Chi <sup>2</sup>	92 147 60 43 15 357 = 17.36	19 47 13 22 7 108 df = 4 /P	147 60 43 15 357	2.5% 1.1% 1.0% 0.2% 6.7%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41]	
I.2.6 isolated CABG Nobaszadeh 2012 Halvorsen 2003 Mirhosseini 2011 reasongsukar 2005 Suezawa 2013 Subtotal (8% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z	32 40 10 9 1 	92 147 60 43 15 357 = 17.36, 2 = 0.27)	19 47 13 22 7 108 df = 4 (P	147 60 43 15 357 = 0.002	2.5% 1.1% 1.0% 0.2% 6.7%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41]	
2.2.6 isolated CABG bbbaszadeh 2012 falvorsen 2003 dirhosseni 2011 rrasongsukarn 2005 Suezawa 2013 subtotal (9% CI) fotal events feterogeneity: Tau <sup>2</sup> = 0 fest for overall effect: Z .2.7 received steroid of	32 40 10 9 1 -58; Chi <sup>2</sup> = 1.11 (F during o	92 147 60 43 15 357 = 17.36, > = 0.27) peration	19 47 13 22 7 108 df = 4 (P	147 60 43 15 357 = 0.002	2.5% 1.1% 1.0% 0.2% 6.7%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41]	
1.2.6 isolated CABG bbbaszadeh 2012 talvorsen 2003 dirhosseini 2011 <sup>2</sup> rasongsukarn 2005 Suezawa 2013 Subtotal (9% CI) Total events teterogeneily: Tau <sup>2</sup> = 0. fest for overall effect: Z 1.2.7 received steroid d Dieleman 2012	32 40 10 9 1 :58; Chi <sup>2</sup> = 1.11 (F during or 259	92 147 60 43 15 357 = 17.36, 2 = 0.27) peration 784	19 47 13 22 7 108 df = 4 (P	147 60 43 15 357 = 0.002 781	2.5% 1.1% 1.0% 0.2% 6.7% 4.7%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.88 [0.01, 0.79] 0.64 [0.29, 1.41]	
1.2.6 isolated CABG bbbaszadeh 2012 talvorsen 2003 dirhossein 2011 Prasongsukam 2005 Suczawa 2013 Subtotal (95% CI) Fotal events teterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.7 received steroid of Dieleman 2012 lacob 2015	32 40 10 9 1 58; Chi <sup>2</sup> = 1.11 (F during oj 259 9	92 147 60 43 15 357 = 17.36, 2 = 0.27) peration 784 30	19 47 13 22 7 108 df = 4 (P 277 12	147 60 43 15 357 = 0.002 781 32	2.5% 1.1% 1.0% 0.2% 6.7% 4.7% 0.9%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.88 [0.01, 0.79] 0.64 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06]	
1.2.6 isolated CABG bbbaszadeh 2012 falvorsen 2003 Michosseni 2011 Prasongsukam 2005 Subcata (9% CI) Total events teterogeneity: Tau <sup>2</sup> = 0 Fest for overall effect: Z 1.2.7 received steroid of bieleman 2012 Jacob 2015 Michosseini 2011	32 40 10 9 1 .58; Chi <sup>2</sup> = 1.11 (F during op 259 9 10	92 147 60 43 15 357 = 17.36, 2 = 0.27) peration 784 30 60	19 47 13 22 7 108 df = 4 (P 277 12 13	147 60 43 15 357 = 0.002 781 32 60	2.5% 1.1% 1.0% 0.2% 6.7% 4.7% 0.9% 1.1%	0.80 [0.48, 1.31] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81]	
1.2.6 isolated CABG Abbaszadeh 2012 talvorsen 2003 Michosseini 2011 Prasongsukam 2005 Suezawa 2013 Subtotal (95% CI) Total events teterogeneity: Tau <sup>2</sup> = 0. fast for overall effect: 2 1.2.7 received steroid i bieleman 2012 Iacob 2015 Michosseini 2011 Suezawa 2015 Mithos 2005	32 40 10 9 1 .58; Chi <sup>2</sup> = 1.11 (F during oj 259 9 10 1 7	92 147 60 43 15 357 = 17.36, 2 = 0.27) peration 784 30 60 15 28	19 47 13 22 7 108 df = 4 (P 277 12 13 7 0	147 60 43 15 357 = 0.002 781 32 60 15	4.7% 0.9% 1.1% 0.2% 6.7% 4.7% 0.9% 1.1% 0.2% 0.8%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.88 [0.01, 0.79]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Mirhosseini 2011 Prasongsukam 2005 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z 1.2.7 received steroid ( Dieleman 2012 Jacob 2015 Mirhosseini 2011 Suszawa 2015 Mithock 2005	32 40 10 9 1 58; Chi <sup>2</sup> = 1.11 (F during of 259 9 10 1 1 7 7 201	92 147 60 43 15 357 = 17.36, > = 0.27) peration 784 30 60 15 28 3755	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846	147 60 43 15 357 = 0.002 781 32 60 15 30 3752	2.5% 1.1% 1.0% 0.2% 6.7% 6.7% 4.7% 0.9% 1.1% 0.2% 0.8% 5.4%	0.80 [0.48, 1.31] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.73 [0.21, 0.29] 0.67 [0.21, 0.29]	
1.2.6 isolated CABG Abbaszadeh 2012 Halvorsen 2003 Withosseini 2011 Prasongsukarn 2005 Subzata (2014 Contained (2014) Prasongsukarn 2005 Subztata (49% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: Z 1.2.7 received steroid ( Joieleman 2012 Jacob 2015 Withosselni 2011 Suezawa 2013 Whitlock 2015 Whitlock 2016	32 40 10 9 1 58; Chi <sup>2</sup> = 1.11 (F during oj 259 9 10 1 7 821 17	92 147 60 43 15 357 = 17.36, > = 0.27) peration 784 30 60 15 28 3755 106	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 36	147 60 43 15 357 = 0.002 781 32 60 15 30 3752 110	2.5% 1.1% 1.0% 0.2% 6.7% 4.7% 0.9% 1.1% 0.2% 0.8% 5.4% 1.8%	0.80 (0.48, 1.31) 0.72 (0.29, 1.81) 0.25 (0.10, 0.65) 0.08 (0.01, 0.79) 0.64 (0.29, 1.41) 0.90 (0.73, 1.11) 0.71 (0.25, 2.06] 0.72 (0.29, 1.81) 0.67 (0.21, 2.09) 0.67 (0.21, 2.09) 0.67 (0.21, 2.09) 0.68 (0.86, 1.07) 0.39 (0.20, 0.78)	
1.2.6 isolated CABG bbbaszadeh 2012 talvorsen 2003 ulrhosseini 2011 Prasongsukam 2005 buczawa 2013 Subtotal (95% CI) Fotal events teterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z J.2.7 received steroid of Joleman 2012 Joleman 2012 Joleman 2013 Whitok 2005 Whitok 2005 Vhitok 2005 Yared 2007	32 40 10 9 1 92 58; Chi <sup>2</sup> = 1.11 (F during oj 259 9 10 1 7 821 17 11	92 147 60 43 15 357 = 17.36, > = 0.27) peration 784 30 60 15 28 3755 106 37	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 366 12	147 60 43 15 357 = 0.002 781 32 60 15 30 3752 110 34	2.5% 1.1% 1.0% 2.5% 1.1% 0.2% 6.7% 4.7% 0.9% 1.1% 0.8% 5.4% 1.8%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.69 [0.20, 0.76] 0.98 [0.20, 2.76]	
1.2.6 isolated CABG bbbaszadeh 2012 falvorsen 2003 dirhosseini 2011 Prasongsukarn 2005 Subotata (95% CI) Total events feterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.7 received steroid at bieleman 2012 Jacob 2015 dirhosseini 2011 Suezawa 2013 Whitlock 2015 Mithock 2015 Mithock 2015 Arared 2000 Subotata (95% CI)	32 40 10 9 1 .58; Chi <sup>2</sup> = 1.11 (F during oj 259 10 1 7 821 17 11	92 147 60 43 15 357 = 17.36, 9 = 0.27) peration 784 30 60 15 28 3755 106 37 4815	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 36 12	147 60 43 15 357 = 0.002 781 32 60 15 30 3752 110 34 4814	2.5% 1.1% 1.0% 0.2% 6.7% 4.7% 4.7% 4.7% 0.9% 1.1% 0.2% 0.8% 1.1% 0.2% 0.8% 1.1% 1.5.9%	0.80 [0.48, 1.31] 0.72 [0.49, 1.31] 0.72 [0.10, 0.65] 0.08 [0.01, 0.79] 0.84 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.65 [0.10, 0.79] 0.67 [0.21, 2.09] 0.66 [0.48, 1.07] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76]	
1.2.6 isolated CABG Abbaszadeh 2012 talvorsen 2003 Michosseini 2011 Prasongsukarn 2005 Suezawa 2013 Suezawa 2013 Suezawa 2013 L.2.7 received steroid of Jaieman 2012 Jacob 2015 Michosseini 2011 Suezawa 2013 Whitlock 2015 Grand 2000 Fared 2000 Fared 2000 Fared 2005 Subtotal (95% CI) Total events	32 40 10 9 1 58; Chi <sup>2</sup> ; 58; Chi <sup>2</sup> ; 58; Chi <sup>2</sup> ; 9 9 10 1 7 821 17 11 1135	92 147 60 43 15 357 = 17.36, 2 = 0.27) peration 784 30 60 15 28 3755 106 37 4815	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 36 12 1213	147 60 43 15 357 = 0.002 781 32 60 15 30 3752 110 34 4814	2.5% 1.1% 0.2% 6.7% 9.2% 6.7% 4.7% 0.9% 1.1% 0.2% 0.9% 1.1% 5.4% 1.8% 1.0% 15.9%	0.80 [0.48, 1.31] 0.72 [0.10, 0.65] 0.25 [0.10, 0.65] 0.80 [0.07, 1.11] 0.84 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.72 [0.29, 1.81] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.67 [0.22, 2.00] 0.80 [0.86, 1.01]	
1.2.6 isolated CABG bbbaszadeh 2012 talvorsen 2003 dirhosseini 2011 Prasongsukam 2005 Subtotal (95% CI) Total events teterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z lacob 2015 Joieleman 2012 Jacob 2015 dirhosseini 2011 Suszawa 2013 Whitlock 2006 Yared 2007 Subtotal (95% CI) Total events teterogeneity: Tau <sup>2</sup> = 0.	32 40 10 9 1 58; Chi <sup>2</sup> = 1.11 (F during oj 259 9 10 1 7 821 77 11 1135 .03; Chi <sup>2</sup>	92 147 60 43 15 357 = 17.36, > = 0.27) peration 784 30 60 15 28 3755 106 37 4815 = 12.47.	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 36 12 1213 df = 7 (P	147 60 43 15 357 = 0.002 781 32 60 15 30 3752 110 34 4814 = 0.09)	2.5% 1.1% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 0.2% 0.2% 0.2% 0.2% 1.1% 0.2% 0.2% 1.1% 0.2% 1.1% 0.2% 1.1% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 6.7% 4.7% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	0.80 [0.48, 1.31] 0.22 [0.10, 0.65] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.68 [0.01, 0.79] 0.67 [0.21, 2.09] 0.69 [0.66, 1.07] 0.59 [0.20, 0.76] 0.78 [0.29, 2.10] 0.80 [0.64, 1.01]	
1.2.6 isolated CABG bbbaszadeh 2012 talvorsen 2003 ulrhosseini 2011 Prasongsukam 2005 Vauzawa 2013 bubtotal (95% CI) Total events teterogeneity: Tau" = 0. rest for overall effect: Z lacob 2015 diritosseini 2011 bieleman 2015 diritosseini 2013 Whitlock 2006 Vhitlock 2015 fared 2007 lubtotal (95% CI) total events teterogeneity: Tau" = 0. rest for overall effect: Z	32 40 10 9 1 58: Chi <sup>2</sup> = 1.11 (F during oj 259 9 10 1 7 821 17 11 1135 .03; Chi <sup>2</sup> = 1.91 (F	92 147 60 43 15 357 = 17.36, > = 0.27) peration 784 30 60 15 28 3755 106 37 4815 = 12.47, > = 0.06)	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 36 12 1213 df = 7 (P	147 60 43 15 357 = 0.002 781 32 60 15 30 3752 110 3752 110 34 4814 = 0.09)	2.5% 1.1% 0.2% 6.7% ); P = 77% 4.7% 0.9% 0.8% 0.8% 5.4% 1.1% 1.8% 15.9% ; P = 44%	0.80 [0.46, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.86 [0.14, 0.79] 0.67 [0.21, 2.09] 0.69 [0.66, 1.07] 0.39 [0.20, 0.76] 0.78 [0.29, 2.10] 0.80 [0.64, 1.01]	
1.2.6 isolated CABG bbbaszadeh 2012 falvorsen 2003 Mirhosseini 2011 Prasongsukarn 2005 Subtotal (95% CI) Total events feterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.7 received steroid a Dieleman 2012 Mirhosseini 2011 Suszawa 2015 Mirhosseini 2011 Suszawa 2013 Whitlock 2015 fared 2000 Fared 2007 Subtotal (95% CI) Total events feterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.8 received steroid a	32 40 10 92 5.58; Chi <sup>2</sup> = 1.11 (F during oj 259 10 1 7 821 17 821 17 11 1135 .03; Chi <sup>2</sup> = 1.91 (F	92 147 60 43 35 357 = 17.36, 9 = 0.27) peration 784 30 60 15 28 3755 106 37 4815 = 12.47, 4815 = 12.47, 9 = 0.6) peration	19 47 13 22 7 7 108 df = 4 (P 277 12 13 7 7 12 13 7 7 10 846 36 12 1213 4f = 7 (P	147 60 43 15 357 = 0.002 781 32 60 0 5 30 3752 100 3752 110 34 4814 = 0.09)	2.5% 1.1% 1.0% 0.2% 6.7% 1.0% 0.2% 0.9% 1.1% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	0.80 [0.46, 1.31] 0.72 [0.49, 1.31] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.84 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.69 [0.68, 1.01] 0.80 [0.64, 1.01]	
1.2.6 isolated CABG Abbaszadeh 2012 talvorsen 2003 Michossein 2011 Prasongsukam 2005 Suczawa 2013 Subtotal (95% CI) Total events teterogeneity: Tau <sup>2</sup> = 0. Teat for overall effect: 2 J.2.7 received steroid d Vinitock 2005 Mittock 2005 Mittock 2005 Mittock 2005 Mittock 2015 fared 2007 Subtotal (95% CI) Total events teterogeneity: Tau <sup>2</sup> = 0. Teat for overall effect: 2 J.2.8 received steroid d Mobaszadeh 2012	32 40 10 9 9 1 255; Chi <sup>2</sup> i 259 9 10 1 7 7 821 17 17 11 5 0.03; Chi <sup>2</sup> i 9 9 10 1 7 7 821 17 11 5 9 9 9 0 0 1 9 9 9 10 1 9 9 9 9 10 10 9 9 9 10 10 9 9 10 10 9 9 10 10 9 9 10 10 9 9 10 10 9 9 10 10 9 9 10 10 9 9 10 10 9 9 10 10 10 9 9 10 10 10 9 10 10 10 10 10 10 10 10 10 10 10 10 10	92 147 60 43 35 357 = 17.36,6 9 = 0.27) peration 784 30 60 015 28 3755 106 615 28 3755 = 12.47, 9 = 0.6) peration 28 37 59 9 = 0.27) 9 = 0.27 10 50 50 50 50 50 50 50 50 50 50 50 50 50	$\begin{array}{c} 19\\ 47\\ 13\\ 22\\ 7\\ \end{array}$ $\begin{array}{c} 108\\ df = 4 \ (P) \\ 277\\ 12\\ 13\\ 7\\ 10\\ 846\\ 36\\ 12\\ 1213\\ df = 7 \ (P) \\ 41213\\ df = 7 \ (P) \\ 19\\ 19\\ \end{array}$	781 327 781 327 357 781 32 60 15 30 3752 110 34 4814 4814 ****************************	2.5% 1.1% 0.2% 6.7% 9.9% 1.1% 0.9% 1.1% 0.8% 5.4% 1.0% 15.9% 1.0% 15.9% 12.4%	0.80 [0.48, 1.31] 0.72 [0.29, 1.81] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.84 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.67 [0.21, 2.09] 0.68 [0.01, 0.79] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.39 [0.29, 2.10] 0.80 [0.64, 1.01]	
1.2.6 isolated CABG bbbaszadeh 2012 talvorsen 2003 dirhosseini 2011 Prasongsukam 2005 Subtotal (95% Cl) Total events teterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z lacob 2015 Joieleman 2012 lacob 2015 dirhosseini 2011 Subtotal (95% Cl) Otal events teterogeneity: Tau <sup>2</sup> = 0. Fared 2007 Subtotal (95% Cl) Total events teterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.7 received steroid d Subtotal (95% Cl) Total events teterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.8 received steroid d Abbaszadeh 2012 4.5 havabkeh 2017	32 40 10 9 1 1 255; Chi <sup>2</sup> 9 9 10 10 7 7 821 17 7 11 17 11 1135 5 6,03; Chi <sup>2</sup> 11 7 7 821 17 7 11 17 13 5 8 259 9 9 3 0 0 0 10 0 9 9 10 0 10 9 9 9 10 0 10 9 10 10 9 9 9 9	$\begin{array}{c} 92\\ 147\\ 60\\ 43\\ 15\\ 357\\ \end{array}$ = 17.36, = 20.27) peration 784 300 15 28 3755 106 3755 106 3755 = 12.47, = 0.06) 92 170 92 170	19 47 13 22 7 108 df = 4 (P 277 7 12 13 7 12 13 7 12 13 3 7 12 13 3 7 12 13 3 7 12 13 3 7 12 13 3 6 5 12 2 2 7 7 13 2 2 2 7 7 13 2 2 2 7 7 13 2 2 2 2 7 7 7 13 2 2 2 2 2 7 7 7 13 2 2 2 2 7 7 7 13 2 2 2 2 7 7 7 10 8 8 10 10 2 7 7 7 10 8 10 10 10 2 7 7 7 10 8 10 10 10 10 10 10 10 10 10 10 10 10 10	781 357 781 32 60 15 30 3752 4814 4814 4814 4814 4814	2.5% 1.1% 1.0% 0.2% 6.7% 6.7% 6.7% 6.7% 6.7% 6.7% 6.7% 6.7	0.80 [0.46, 1.31] 0.25 [0.10, 0.65] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.28, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.28, 1.81] 0.71 [0.25, 2.06] 0.72 [0.28, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.71 [0.25, 2.06] 0.72 [0.29, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 2.10] 0.80 [0.64, 1.01] 2.05 [1.06, 3.97] 0.43 [0.27, 0.70]	
1.2.6 isolated CABG Abbaszadeh 2012 talvcrsen 2003 Michosseini 2011 Prasongsukarn 2005 Suezava 2013 Subtotal (95% CI) Total events teterogeneity: Tau <sup>2</sup> = 0 teterogeneity: Tau <sup>2</sup> = 0 teterogeneity: Tau <sup>2</sup> = 0 Jeleman 2012 Jacob 2015 Mintock 2015 Grand 2000 Fared Fared Fare	32 40 10 9 1 259 58; Chi <sup>2</sup> = 1.11 (F during of 821 17 11 11 35 60,3; Chi <sup>2</sup> = 1.91 (F during of 32 36 6 9 9	$\begin{array}{c} 92\\ 147\\ 60\\ 43\\ 15\\ 357\\ = 17.36, \\ 2 = 0.27)\\ \\ peration\\ 784\\ 30\\ 60\\ 15\\ 28\\ 3755\\ 28\\ 3755\\ 106\\ 37\\ 4815\\ = 12.47, \\ 2 = 0.06)\\ \\ peration\\ 92\\ 170\\ 52\\ \end{array}$	19 47 13 22 7 108 df = 4 (P 277 12 13 7 10 846 36 12 1213 36df = 7 (P 9 9 65 5 14	781 327 781 322 60 15 30 3752 110 34 4814 4814 92 170 52	2.5% 1.1% 0.2% 6.7% 6.7% 4.7% 0.9% 1.1% 0.2% 0.9% 1.1% 0.2% 0.8% 5.4% 1.0% 15.9% 15.9% 15.9% 15.9% 1.1%	0.80 [0.48, 1.31] 0.22 [0.10, 0.65] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.84 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.67 [0.21, 2.09] 0.76 [0.21, 2.09] 0.76 [0.21, 2.09] 0.76 [0.22, 2.10] 0.39 [0.20, 0.76] 0.78 [0.29, 2.10] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.39 [0.20, 0.76] 0.43 [0.27, 0.70] 0.43 [0.27, 0.70]	
1.2.6 isolated CABG hbbaszadeh 2012 Halvorsen 2003 Wirhosseini 2011 Prasongsukam 2005 Suezava 2013 Subtotal (95% CI) Total events Heterogeneity: Tau" = 0. Test for overall effect: Z 1.2.7 received steroid of Dieleman 2012 Jacob 2015 Wirhosseini 2011 Suezava 2013 Whitock 2006 Whitock 2006 Whitock 2015 Yared 2007 Subtotal (95% CI) Total events Heterogeneity: Tau" = 0. Test for overall effect: Z 1.2.8 received steroid of Hobaszadeh 2012 Abbaszadeh 2012	32 40 10 9 1 1 58; Chi <sup>2</sup> H 259 9 9 10 1 1 259 9 9 10 0 1 1 7 7 821 17 17 11 11 11 5.03; Chi <sup>2</sup> H 259 9 9 10 0 1 1 259 9 9 10 1 259 9 9 10 10 10 9 9 10 10 9 9 10 10 10 9 9 10 10 10 9 9 10 10 10 9 9 10 10 10 9 9 10 10 10 10 9 9 10 10 10 10 9 9 10 10 10 10 9 9 10 10 10 10 10 9 9 10 10 10 10 10 10 10 10 10 10 10 10 10	$\begin{array}{c} 92\\ 147\\ 60\\ 43\\ 15\\ 357\\ = 0.27\\ \end{array}$	$\begin{array}{c} 19\\ 47\\ 13\\ 22\\ 7\\ 108\\ df = 4 \ (P\\ 277\\ 12\\ 13\\ 7\\ 12\\ 13\\ 7\\ 12\\ 13\\ df = 7 \ (P\\ 19\\ 65\\ 14\\ 62\\ \end{array}$	781 327 781 32 357 781 32 30 3752 110 33 34 4814 4814 4814 92 92 170 0 52 127	2.5% 1.1% 1.0% 0.2% 6.7% 4.7% 6.7% 4.7% 0.8% 1.1% 1.0% 1.0% 1.0% 1.8% 1.0% 1.5.9% 1*5.9% 1*5.9% 1*5.9%	0.80 [0.46, 1.31] 0.25 [0.10, 0.65] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.64 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.61] 0.71 [0.25, 2.06] 0.72 [0.29, 1.61] 0.73 [0.29, 2.06] 0.76 [0.74, 2.09] 0.65 [0.26, 1.07] 0.45 [0.29, 2.10] 0.86 [0.46, 1.07] 0.80 [0.64, 1.01]	
1.2.6 isolated CABG bbbaszadeh 2012 falvorsen 2003 Mirhosseini 2011 Prasongsukam 2005 Subtotal (95% CI) Total events feterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.7 roceived steroid ( Dieleman 2012 facob 2015 Mirhosseini 2011 Subzawa 2015 Mirhosk 2015 fared 2000 Fared 2007 Subtotal (95% CI) Total events feterogeneity: Tau <sup>2</sup> = 0. Fest for overall effect: Z 1.2.8 received steroid ( bbbaszadeh 2012 4.5Rawabkeh 2017 Somez Polo 2017 falonen 2007 Talovrsen 2003	32 40 10 9 9 22 58; Chi <sup>2</sup> i 11 9 259 9 9 10 1 1 7 7 821 17 7 11 135 5 821 14 9 10 10 17 7 821 17 7 821 11 9 9 9 9 9 10 10 9 10 9 9 9 9 9 9 10 10 9 10 9 259 9 9 10 10 9 10 9 10 9 259 9 9 10 10 10 9 10 9 10 9 10 9 10 10 9 10 9 10 10 9 10 9 10 10 9 10 10 9 10 10 9 10 10 10 9 10 10 10 9 10 10 10 10 10 10 10 10 10 10 10 10 10	92 147 60 43 15 357 = 17.36, 0 = 0.27) peration 784 30 60 015 28 3755 28 3755 = 12.47, 0 = 0.06) 92 92 - 0.06) 92 - 0.06)	19 47 13 22 7 108 df = 4 (P 277 12 13 13 36 12 1213 36 12 1213 36 12 1213 36 12 1213 36 12 1213 12 12 13 16 12 12 12 13 13 12 12 13 13 12 12 13 13 13 13 13 13 13 13 13 13 13 13 13	781 32 60 3357 357 357 30 3752 30 3752 30 3752 30 3752 100 34 4814 = 0.09) 3752 110 0 34 4814 10 52 127 70 127 147	2.5% 1.1% 2.5% 1.1% 0.2% 6.7% 6.7% 4.7% 0.9% 1.1% 0.9% 1.1% 0.8% 5.4% 1.0% 15.9% 15.9% 15.9% 11.8% 1.2.7% 1.1% 2.5%	0.80 [0.46, 1.31] 0.72 [0.10, 0.65] 0.25 [0.10, 0.65] 0.08 [0.01, 0.79] 0.84 [0.29, 1.41] 0.90 [0.73, 1.11] 0.71 [0.25, 2.06] 0.72 [0.29, 1.81] 0.67 [0.21, 2.09] 0.45 [0.10, 0.8, 1.01] 0.80 [0.46, 1.01] 2.05 [1.06, 3.97] 0.43 [0.27, 0.70] 0.43 [0.27, 0.70] 0.43 [0.27, 0.70] 0.43 [0.27, 0.70]	
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Figure 7. Forest plot for subgroup analyses of postoperative atrial fibrillation.

development of AF is not well known. The anti-inflammatory activity of CSs may play the vital role of preventing POAF. All markers of increased inflammatory reaction concentration, such as complement C-reactive protein complex, white blood cells, inflammatory cytokines, are higher in patients with POAF than in patients who remain in sinus rhythm after cardiac surgery.<sup>[2]</sup> The concentration of C-reactive protein was significantly lower postoperatively in the steroid group than in the placebo group.<sup>[2,12,15,18]</sup> Another possible effect of steroids is that CSs reduce postoperative nausea, vomiting, and anorexia. Thus, CS therapy may improve absorption of oral medications, such as -blockers, and thereby reduce the incidence of AF.<sup>[16]</sup>

Interestingly, the subgroup analysis shows that a medium dose of CSs was associated with reducing the incidence of POAF compared with low doses. A possible explanation for this might be that fewer studies using low or high doses of CS, so that low and high doses of steroid in these studies did not have prophylactic effects on AF. Another reason is the response of CS therapy, which is in normal distribution (bell curve) where the optimum effective dose is the medium. Furthermore, the antiinflammatory effects are dose-dependent, according to the pharmacology.<sup>[21]</sup> However, high dose of steroid has the potential risks of increasing side effects. Some previous metaanalyses also investigating that low- and high-dose CSs were ineffective in preventing AF in contrast to moderate doses.<sup>[22,23]</sup> This fact was confirmed in our meta-analysis that optimum dose was the medium one.

Compared with different types of CSs, maybe, methylprednisolone could be better candidate to reduce the incidence of POAF according to this meta-analysis, although there was not statistically significant difference. Therefore, no firm conclusions can be drawn here, because of the limitations of the subgroup analysis.

There are several reasons that might explain why some studies could not demonstrate any protective effect of CSs on postoperative AF. One possible reason is that the moment and duration of steroid administration. Previous studies which demonstrating a protective effect of steroid treatment on POAF were designed to administer steroid not only preoperatively, but also on the following days of surgery. Other trials just gave a single shot shortly after the induction of anesthesia or during the surgery process. In our subgroup analysis, we did not see the significant difference between administration at variety perioperative moments. The optimal timing of drug delivery and the frequency of administration remain unclear.

One large RCT and a recent systematic review indicate that prophylactic administration of steroid is associated with an increase in myocardial infarction or injury.<sup>[9,24]</sup> However, the increase in myocardial injury with steroid in these studies was not reported in other previous trials. The reason of this contradicted result may mainly because of differing MI definitions which can impacted the event incidence between trials. Taking the 2 large clinical trials (Steroids In caRdiac Surgery study [SIRS] and Dexamethasone for Cardiac Surgery Study [DECS]) as examples, in the SIRS trial that mandated postoperative creatinine kinasefraction myocardial band and Electrocardiograph monitoring, the overall incidence of myocardial injury was 11.8%.<sup>[8,9]</sup> In contrast, in the DECS trial, MIs were defined by a biomarker elevation in association with new Q-waves or left bundle branch block on Electrocardiograph, which resulted in a much lower incidence of 1.7%. our meta-analysis did not see the evidence that steroid administration can impact the incidence of myocardial injury after cardiac surgery.

The findings of our study demonstrated that CS receivers had a statistically reduction on the length of hospital stay, which indeed depends on reduction of surgical complications and improvement in clinical outcomes after CABG. There are other meta-analysis supporting our finding.<sup>[1,25]</sup> However, steroid prophylaxis had no effect on reducing the length of ICU stay and did not increase the time of need for mechanical ventilation. In agreement with our study, Cappabianca et al also reported that steroids could reduce morbidity, surgical complications, and Hospital Length of Stay.<sup>[6]</sup>

One of the potential risks of applying CS perioperatively is that steroid-induced suppression could significantly increase the risk of infection. Our study indicated that administration of steroid did not increase any infections at all. In addition, there was no statistical difference in the rate of major complication between the steroid and the placebo groups on high blood sugar level, gastrointestinal complications, postoperative bleeding, and delirium. According to our meta-analysis, we believe that using steroid in perioperative moments with low or medium doses are safety in patients undergoing CABG alone or combined with valve surgery.

Our analysis included 2 large clinical trials (SIRS and DECS) which contribute about 12,000 patients to the total 13,803 patients.<sup>[8,9]</sup> Therefore, our results are mostly based on these 2 large high quality RCTs, and more multicentric large clinical trials are needed to confirm our meta-analysis findings.

There are several limitations in our study. First, a major limitation of this meta-analyses is the heterogeneity of the included studies. Some results of our meta-analysis have significant heterogeneities. Most of these studies were small in sample size (18-294 patients) and investigated various types of CSs in multiple doses at different time points of administration. Second, definitions of end points were different across included studies, such as myocardial infarctions, which threatens the validity of our results. The low event rates and the small proportion of trials reporting outcomes limit our ability to draw conclusions about the effect of steroids on these outcomes. Moreover, we did not have access to further propensity analysis or stratified analysis to better define differences between treatment groups. Finally, we would also like to point out the publication bias exaggerating the positive effects when metaanalysis was based on previously published studies, due to positive results are more tendency to be published than negative results.

In conclusion, the present meta-analysis suggests a beneficial effect of steroids to prevent new-onset atrial fibrillation after cardiac surgery. Steroid prophylaxis in patients undergoing CABG or combine with valve surgery could significantly reduce the incidence of new-onset POAF, and the length of hospital stay. On the other hand, it is an effective safe treatment that does not increase the incidence of infection or other side effects of steroids compared with the placebo. The strength of this relationship should be interpreted with caution because of statistical and clinical heterogeneity among the included studies.

#### Author contributions

Conceptualization: Xiao-Wen Wang.

Data curation: Lu Liu, Xiao-Wen Wang.

Formal analysis: Lu Liu, Fu-Yu Jing, Lin-Jun Li.

Methodology: Lu Liu, Fu-Yu Jing, Lin-Jun Li, Rui-Qin Zhou, Cheng Zhang. Project administration: Chen Zhang, Rui-Qin Zhou, Xiao-Wen Wang.

- Software: Fu-Yu Jing, Lin-Jun Li, Lu Liu, Rui-Qin Zhou, Cheng Zhang.
- Supervision: Xiao-Wen Wang, Qing-Chen Wu.

Validation: Cheng Zhang.

Writing – original draft: Lu Liu.

Writing - review & editing: Xiao-Wen Wang, Qing-Chen Wu.

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