CJC Open 4 (2022) 85–96

Systematic Review/Meta-analysis

Short-term and Long-term Risk of Stroke in Patients With Perioperative Atrial Fibrillation After Cardiac Surgery: Systematic Review and Meta-analysis

Michael K. Wang, MD,[a,b,c] Pascal B. Meyre, MD, PhD,[d] Rachel Heo, BHSc,[e] P.J. Devereaux, MD, PhD,[a,b,c] Lauren Birchenough,[f] Richard Whitlock, MD, PhD,[b,c,g] William F. McIntyre, MD, PhD,[a,b,c] Yu Chiao Peter Chen, MD,[h] Muhammad Zain Ali,[i] Fausto Biancari, MD, PhD,[j] Jawad Haider Butt, MD,[k] Jeff S. Healey, MD, MSc,[a,b,c] Emilie P. Belley-Côté, MD, PhD,[a,b] Andre Lamy, MD, MHSc,[b,c,g] and David Conen, MD, MPH[a,b,c]

[a] *Department of Medicine, McMaster University, Hamilton, Ontario, Canada;* [b] *Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada;* [c] *Department of Health Research Methods, Evidence & Impact, McMaster University, Hamilton, Ontario, Canada;* [d] *Division of Cardiology and Basel Cardiovascular Research Institute, Basel University Hospital, Basel, Switzerland;* [e] *Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada;* [f] *Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada;* [g] *Department of Surgery, McMaster University, Hamilton, Ontario, Canada;* [h] *Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada;* [i] *School of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland;* [j] *Clinica Montevergine, GVM Care & Research, Mercogliano, Italy;* [k] *Department of Cardiology, Rigshopitalet, Copenhagen University Hospital, Copenhagen, Denmark*

ABSTRACT

Background: Perioperative atrial fibrillation (POAF) after cardiac surgery has been associated with an increased risk of stroke in some studies. However, the exact magnitude of this association during short-term and long-term follow-up remains unclear.

Methods: We searched PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) for the time period from database inception to October 2020. We included observational studies with ≥ 100 patients that reported data on short-term or long-term stroke risk in patients with and without POAF after cardiac surgery. Data were pooled

RÉSUMÉ

Contexte : La fibrillation auriculaire périopératoire (FAPO) après une chirurgie cardiaque a été associée à un risque accru d'accident vasculaire cérébral (AVC) dans certaines études. Cependant, l'ampleur exacte de cette association durant le suivi à court et à long terme reste incertaine.

Méthodologie : Nous avons effectué des recherches dans les bases de données PubMed, Embase et CENTRAL (Cochrane Central Register of Controlled Trials) pour la période allant de la création de ces bases à octobre 2020. Nous avons inclus des études d'observation

The incidence of perioperative atrial fibrillation (POAF) after cardiac surgery ranges between 20% and 40%.[1,2] POAF usually occurs within the first several days after surgery,[3] and it is believed to be triggered by a combination of surgical (eg, acute inflammation) and patient-related factors (eg, obesity, hypertension).[4] As most patients with POAF convert back to sinus rhythm prior to hospital discharge,[5] many clinicians consider POAF to be a transient and self-limited event.[6] However, a growing body of evidence suggests that POAF is associated with an increased risk of stroke even after hospital discharge.

The increased stroke risk seen in patients with POAF may be mediated in part by subsequent episodes of atrial fibrillation (AF).[7] Given this, some clinicians prescribe oral anticoagulation to patients with POAF in order to mitigate their stroke risk.[8] However, whether the observed increase in stroke risk persists beyond the immediate perioperative period is unclear. Although most observational studies have shown an association between POAF and short-term stroke risk,[9-11] conflicting results among published studies have raised uncertainty as to whether the association persists during

Received for publication July 10, 2021. Accepted September 12, 2021.

Ethics Statement: This systematic review and meta-analysis was conducted in accordance to the ethical principles described in the Declaration of Helsinki.

Corresponding author: Dr Michael K. Wang, 237 Barton St East, Hamilton, Ontario L8L 2X2, Canada. Tel.: +1-289-426-2472; fax: +1-365-317-6272.

E-mail: wangm7@mcmaster.ca

See page 94 for disclosure information.

https://doi.org/10.1016/j.cjco.2021.09.011

using random-effects models. We reported summary risk ratios (RRs) for studies reporting multivariable adjusted results and calculated absolute risk differences (ARDs) with 95% confidence intervals (CIs).
Results: A total of 55 studies with 540,209 patients were included. POAF was associated with both an increased relative risk (RR 1.69; 95% CI, 1.41-2.03; $I^2 = 82\%$; 9 studies) and absolute risk of short-term stroke (4.5% vs 2.5%; ARD 2.0%; 95% CI, 1.28-2.89). POAF was associated with an increased relative risk (RR 1.20; 95% CI, 1.12-1.29; $I^2 = 16\%$; 10 studies) and absolute risk of long-term stroke (1.06 vs 0.88 per 100 patient-years; ARD 0.18 per 100 patient-years; 95% CI, 0.07-0.26). Sensitivity analyses of high-quality studies and studies reporting either ischemic or embolic strokes yielded similar findings.
Conclusions: POAF after cardiac surgery was associated with an increased risk of both short-term and long-term stroke. However, the long-term stroke ARD was small, and whether these patients will benefit from long-term oral anticoagulation therapy is unclear.

comptant $\geq$ 100 patients et rapportant des données sur le risque d'AVC à court ou à long terme chez les patients ayant présenté ou non une FAPO après une chirurgie cardiaque. Les données ont été regroupées à l'aide de modèles à effets aléatoires. Nous avons consigné les rapports de risque (RR) sommaires pour les études rapportant des résultats corrigés multivariables et calculé les différences de risque absolu (DRA) avec des intervalles de confiance (IC) à 95 %.
Résultats : Au total, 55 études portant sur 540 209 patients ont été incluses. La FAPO était associée à une augmentation tant du risque relatif (RR : 1,69; IC à 95 % : 1,41 à 2,03; $I^2 = 82$ %; 9 études) que du risque absolu d'AVC à court terme (4,5 % vs 2,5 %; DRA : 2,0 %; IC à 95 % : 1,28 à 2,89). La FAPO était également associée à une augmentation du risque relatif (RR : 1,20; IC à 95 % : 1,12 à 1,29; $I^2 = 16$ %; 10 études) et du risque absolu d'AVC à long terme (1,06 vs 0,88 par 100 années-patients; DRA : 0,18 par 100 années-patients; IC à 95 % : 0,07 à 0,26). Les analyses de sensibilité des études de haute qualité et des études rapportant des AVC ischémiques ou emboliques ont donné des résultats similaires.
Conclusions : La FAPO après une chirurgie cardiaque a été associée à un risque accru d'AVC à court et à long terme. Cependant, comme la différence de risque absolu d'AVC à long terme était faible, la possibilité qu'une anticoagulothérapie orale à long terme soit bénéfique pour ces patients est incertaine.

long-term follow-up.[3,12-14] Defining the exact magnitude of the excess stroke risk in patients with POAF is crucial in order to determine whether anticoagulation has a meaningful effect that outweighs the risks of bleeding. To address these issues, we performed a systematic review and meta-analysis evaluating the short-term and long-term relative and absolute risks of stroke in patients with POAF after cardiac surgery.

Methods

This systematic review and meta-analysis is reported according to the **M**eta-analyses **o**f **O**bservational **S**tudies in **E**pidemiology (MOOSE) reporting guidelines.[15] The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42020170568).

Search methods

Relevant studies were identified through a systematic literature search of PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from the time of database inception until October 26, 2020. Eligible studies were identified using a search strategy combining keywords and terms related to cardiac surgery, AF, and stroke (Supplemental Appendix S1). Additional articles were identified through reviewing reference lists from relevant studies and consulting experts in the field.

Study selection and outcome assessment

Observational studies and observational analyses from randomized controlled trials were considered eligible for inclusion. Studies were included if they (i) had patients undergoing cardiac surgery; (ii) reported stroke outcomes stratified by the presence or absence of POAF; (iii) defined POAF as a new-onset AF episode; (iv) had $\geq$ 100 participants; and (v) only included patients $\geq$ 18 years of age. The following were excluded: (i) studies of transcatheter valve implantation procedures; (ii) studies that did not distinguish between short-term and long-term strokes; and (iii) studies not published as full-text articles (eg, meeting abstracts). Studies were not excluded on the basis of publication language. Screening and full-text review were conducted independently and in duplicate by 6 of the authors (M.K.W., P.M., R.H., L.B., Y.C.P.C., M.Z.A), with discrepancies resolved through consensus or by consulting with a third independent reviewer.

The primary outcome was stroke. Acceptable definitions of stroke included any stroke, ischemic stroke, and embolic stroke. When multiple types of stroke were reported, we used the outcome of ischemic stroke. We collected information on short-term and long-term stroke risk separately. Short-term strokes were defined as events occurring either in-hospital or within the first 30 days after surgery. Long-term strokes were events occurring either after discharge or more than 30 days after surgery.

Data extraction

Data extraction was performed independently and in duplicate (M.K.W., P.M., R.H., L.B., Y.C.P.C., M.Z.A) using structured forms. Information was collected on study design, sample size, types of surgical procedures, baseline demographics, definitions for POAF and stroke, number of patients with POAF and stroke, reported associations between POAF and stroke, covariates used for multivariable adjustment, and anticoagulation use. If several multivariable models were available, results were extracted from the most adjusted model. We contacted study authors to obtain missing data, unpublished data with multivariable adjustment, and clarifications regarding the number and timing of strokes.

Assessment of the quality of evidence

The Newcastle—Ottawa Scale (NOS) was used to assess the quality of observational studies. This scale assigns a maximum

of 9 points in 3 domains: selection of study groups, comparability of groups, and ascertainment of exposures and outcomes.[16] Quality assessment was completed independently and in duplicate. Disagreements were resolved through consensus, consistent with the process outlined for study eligibility. Studies were considered high quality if they received ≥ 7 points.

Statistical analysis

Separate meta-analyses were constructed for short-term and long-term stroke risk. For our main meta-analyses, we included only studies reporting multivariable adjusted data. Pooled risk ratios (RRs) and their corresponding 95% confidence intervals (CIs) were estimated using the inverse variance method with random-effects models. We used tests of interaction to determine whether there were significant differences between subgroups of studies with and without multivariable adjustment. We additionally reported the pooled RRs across all studies when no significant differences were reported between adjusted and unadjusted subgroups. Between-study statistical heterogeneity was quantified using the I^2 value. Heterogeneity was considered to be important when I^2 was greater than 30%.[17] Publication bias was assessed with Egger's regression test[18] and visual inspection of funnel plots, and corrected using the trim-and-fill method.[19]

The absolute risk difference (ARD) and its corresponding 95% CIs were calculated for short-term and long-term stroke using methods described in the Cochrane Handbook for Systematic Reviews of Interventions.[20] We estimated the baseline short-term and long-term absolute risks of stroke by calculating an overall weighted incidence of stroke in patients without POAF across all included studies. We estimated the absolute risk of stroke and its corresponding 95% CIs in patients with POAF by adding the absolute risk difference and its corresponding 95% CIs to the baseline risk estimate.

We planned several analyses a priori to identify potential sources of heterogeneity. We performed subgroup analyses based on the type of surgical procedure performed (ie, isolated coronary artery bypass surgery (CABG) vs valvular procedures) for short-term and long-term risks of stroke. For studies reporting long-term risk of stroke, we performed univariable meta-regression analyses using a series of predetermined variables that were reported by at least 10 studies, including anticoagulation use, length of follow-up, study size, mean age, and female sex (%). To assess the robustness of our findings, we performed sensitivity analyses by limiting analyses to studies deemed to be of high quality, studies reporting either ischemic or embolic strokes, studies published in the year 2010 or later, and studies that reported the method by which POAF was detected. All analyses were conducted using Review Manager (Cochrane Collaboration, London, UK), version 5.4, or Stata (StataCorp, LLC, College Station, TX), version 16. Analyses were 2-tailed with statistical significance set at $P < 0.05$.

Results

Study selection

Through database searching, reviewing the bibliographies of relevant literature, and consulting with field experts, 14,535 unique citations were identified. After review of the full text of 578 articles, 55 studies were identified as meeting eligibility criteria.[1-3,9-13,21-66] Of the 539,520 participants included, 151,856 (28.1%) had POAF. A flow diagram of the study selection process is shown in Figure 1. Three studies with a total of 443 participants reported no strokes,[55,65,66] leaving 52 studies eligible for inclusion in the meta-analysis. Three primary study authors provided unpublished information on the number of short-term and long-term strokes.[46,48,60] Unpublished outcome data with multivariable adjustment were provided by primary study authors for 4 studies.[3,12,30,46]

Study characteristics

The characteristics of the 55 included studies are outlined in Table 1. The average participant age was 65.8 years (standard deviation: 11.4), and 29.8% were female. Most studies were conducted in North America (33%), Europe (28%), and Asia (19%). Short-term stroke risk was reported in 48 studies, of which 9 reported multivariable adjusted results. Long-term stroke risk was reported in 19 studies, of which 10 reported multivariable adjusted results. In the studies reporting long-term stroke risk, follow-up ranged from 1 to 17.8 years (median: 2.4 years). Studies included patients undergoing isolated CABG surgery (35 studies), valvular surgery with or without a concomitant procedure (11 studies), or a combination of different cardiac procedures (9 studies). A total of 36 studies made the diagnosis of POAF, using either continuous telemetry monitoring or an electrocardiogram. Of the remaining studies, 10 used database records, 2 used medical records, and 7 did not specify how the diagnosis was obtained. A total of 46 studies reported a composite of all strokes; 8 reported ischemic strokes; and 1 reported embolic strokes. For the diagnosis of stroke, 6 studies required imaging findings, 8 studies required compatible clinical findings, 23 studies used diagnoses registered in databases, and 12 studies did not specify a data source.

Quality of studies

Among all 55 studies included in the review, 8 of 48 studies (17%) that reported short-term stroke and 13 of 19 studies (68%) that reported long-term stroke were determined to be high-quality studies (Supplemental Table S1). Fourteen studies (25%) reported follow-up data that were at least 90% complete, and 18 studies (33%) used diagnostic criteria that demonstrated recorded strokes were new events. Among studies that reported multivariable adjusted results, 6 of 9 studies (67%) that reported short-term stroke, and 10 of 10 studies (100%) that reported long-term stroke were determined to be high-quality studies.

Risk of short-term stroke

Among studies that reported short-term stroke risk, 30.1% of participants had POAF (48 studies; Supplemental Table S2). The incidence of POAF was higher among participants undergoing valvular procedures (49.0%; 9 studies), compared to those undergoing isolated CABG (24.3%; 31 studies).

Among studies that reported multivariable adjusted results, the relative risk of short-term stroke was significantly higher in patients with POAF (RR 1.69; 95% CI, 1.41-2.03; 9 studies).

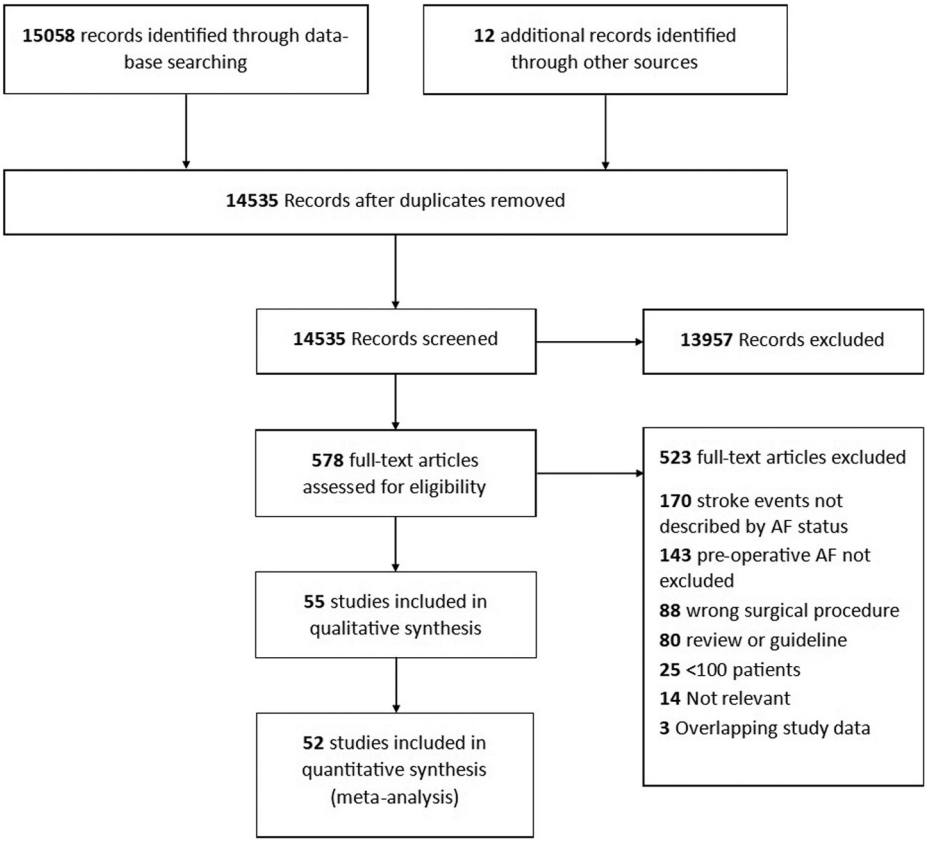

Figure 1. **P**referred **R**eporting **I**tems for **S**ystematic Reviews and **M**eta-**A**nalyses (PRISMA) flow diagram for eligible studies. AF, atrial fibrillation.

Substantial heterogeneity was detected across study results ($I^2 = 82\%$). There was no evidence of publication bias (Egger test, $P = 0.48$). Studies reporting unadjusted results had a higher pooled relative risk (RR 2.22; 95% CI, 1.87-2.63; $I^2 = 61\%$; 39 studies) compared to studies with multivariable adjustment (test for interaction, $P = 0.03$; Fig. 2). The estimated incidence of short-term stroke was 4.5% vs 2.5% in patients with and without POAF (ARD 2.0%; 95% CI, 1.28-2.89; Fig. 3).

Risk of long-term stroke

Among studies that reported long-term stroke risk, 19.7% of participants had POAF (18 studies; Supplemental Table S2). The incidence of POAF was higher among patients undergoing valvular procedures (44.9%; 3 studies), compared with those undergoing isolated CABG (27.3%; 13 studies).

Among studies that reported multivariable adjusted results, the overall risk of long-term stroke was significantly increased in patients with POAF (RR 1.20; 95% CI, 1.12-1.29; 10 studies; Fig. 4). Although between-study heterogeneity was low ($I^2 = 16\%$), we found evidence of publication bias (Egger test, $P = 0.05$). The RR after study imputation by the trim-and-fill method was 1.18 (95% CI, 1.10-1.26; Supplemental Fig. S1). Results remained similar after pooling both unadjusted and adjusted studies (RR 1.24; 95% CI, 1.13-1.35; 18 studies; Fig. 4). The estimated incidence of long-term stroke was 1.06 vs 0.88 per 100 patient-years in patients with and without POAF (ARD 0.18 per 100 patient-years; 95% CI, 0.07-0.26; Fig. 2).

Anticoagulation use

Patients with POAF were more frequently discharged on anticoagulation, compared with those without POAF (11 studies; n = 50,522; 17.7% vs 4.4%; Supplemental Table S3). The average level of use of long-term anticoagulation in patients with vs without POAF was 6.3% and 2.5%, respectively (2 studies; mean follow-up 5.1 years).[14,21]

Meta-regression and sensitivity analyses

In the subgroup analysis comparing the risk of short-term stroke across different types of surgery, isolated CABG was associated with a higher relative risk of short-term stroke (RR 2.17; 95% CI, 1.89-2.49) than valvular surgery (RR 1.52; 95% CI, 1.15-2.02) (P for interaction = 0.03). This difference was not seen among studies reporting long-term stroke risk (P for interaction = 0.13; Supplemental Table S4). Univariable meta-regression analyses did not demonstrate differential associations in the risk of long-term stroke according to follow-up duration or study size (Supplemental Table S5). A post hoc analysis of long-term stroke studies found that the absolute risk of stroke per 100 patient-years was greater in studies reporting a higher prevalence of previous stroke among patients with POAF (upper vs lower tertile of studies; independent t-test $P = 0.02$; Supplemental Fig. S2).

Table 1. Characteristics of included studies

Author	Year	Country	Surgery type	N	POAF (% incidence)	Age (POAF / no POAF)	Female sex (%) (POAF / no POAF)	Stroke outcomes (short-term / long-term)	Multivariable adjusted r esults (short-term / long-term)	Follow-up (years)
Ahlsson[21]	2010	Sweden	Isolated CABG	571	28.9	69 / 65	18.8 / 22.9	- / *	- / -	6.9
Al-Khatib[22]	2009	USA	Isolated CABG	2794	23.7	67 / 61	18.6 / 21.2	* / -	- / -	—
Almassi[24]	1997	USA	CABG, valvular, combination, other	3855	29.7	67 / 62	1.14 / 1.73	* / -	- / -	—
Almassi[23]	2019	USA	Isolated CABG	2103	26.2	65 /62	0.1	* / *	- / -	5
Attaran[25]	2011	UK	CABG, valvular, combination, other	17379	28.7	68 / 64	25.4 / 26.5	* / -	* / -	—
Auer[26]	2005	Austria	Valvular ± CABG	253	39.1	68 / 64	44.5 / 37.0	* / -	- / -	—
Barbieri[27]	2013	Portugal	Isolated CABG	2628	12.4	67 / 61	26.7 / 30.6	* / -	- / -	—
Batra[28]	2019	Sweden	Isolated CABG	8370	27.4	70 / 66	17.4 / 19.3	- / *	- / *	2.2
Benedetto[29]	2020	International	Isolated CABG	3023	24.2	66 / 63	13.5 / 14.5	* / *	- / *	10
Biancari[30]	2013	Finland	Isolated CABG	1226	31.3	67 / 62	28.4 / 25.4	* / *	* / *	7.2
Bramer[31]	2010	The Netherlands	Isolated CABG	5098	22.0	69 / 64	21.2 / 22.5	* / -	- / -	—
Bramer [32]	2011	The Netherlands	MVR ± (CABG or TVR)	856	42.2	67 / 63	37.4 / 41.4	* / -	- / -	—
Butt[3]	2019	Denmark	Isolated valvular	1528	46.6	71 / 68	41.4 / 38	- / *	- / *	4.7
Butt[12]	2018	Denmark	Isolated CABG	7121	30.3	68/ 64	17.7 / 17.9	- / *	- / *	5.5
Choi[33]	2009	South Korea	Isolated CABG	315	21.0	67 / 65	25.8 / 29.3	* / -	- / -	—
Coletta[33]	2019	USA	Isolated CABG	158	29.5	—	16.7 / 30.3	* / -	- / -	—
Conen[14]	2020	Canada	Isolated CABG	4624	16.8	71 / 66	19.8 / 19.2	* / *	- / *	4.4
Echahidi[35]	2007	Canada	Isolated CABG	5085	27.0	68 / 63	23.0 / 23.8	* / -	- / -	—
El-Chami[9]	2010	USA	Isolated CABG	16169	18.5	68 / 61	26.9 / 28.3	* / -	- / -	—
Farouk Musa[36]	2018	Malaysia	Isolated CABG	637	28.7	62 / 60	20.8 / 17.2	* / -	- / -	—
Ghurram[38]	2020	India	Isolated CABG	748	17.0	—	—	* / *	- / -	1.7
Gialdini[37]	2014	USA	CABG, valvular, combination, other	73543	16.1	—	—	- / *	- / *	1
Girerd[39]	2012	Canada	Isolated CABG	6728	27.8	68 / 63	22.6 / 22.0	* / -	- / -	
Guenancia[40]	2015	France	Isolated CABG	100	34.0	66 / 63	8.8 / 6.1	* / *	- / -	1
Horwich[41]	2013	Canada	Isolated CABG	8058	27.5	—	22.7 / 25.3	* / *	- / *	5.7
Hravnak[42]	2002	USA	Isolated CABG	814	31.9	70 / 64	29.6 / 34.5	* / -	- / -	—
Hu[43]	2015	China	Isolated AVR	107	34.6	56 / 50	62.2 / 58.6	* / -	- / -	—
Iliescu[44]	2018	Romania	Isolated AVR	1191	28.7	69 / 64	36.8 / 30.2	* / -	- / -	—
Kalra[45]	2019	USA	Isolated AVR	122765	50.1	72 / 64	38.1 / 40.0	* / -	* / -	—
Kalra (validation cohort)[45]	2019	USA	Isolated AVR	5141	30.6	72 / 65	41.4 / 41.3	* / -	* / -	—
Kim[46]	2020	South Korea	AVR ± other	296	52.0	67	44.9	* / -	* / -	
Kohno[47]	2017	Japan	AVR ± other	157	36.9	71 / 67	46.6 / 49.5	- / *	- / -	4.4
Konstantino[48]	2016	Israel	Isolated CABG	136	27.2	76 / 70	32.4 / 19.2	* / *	- / -	8.5
Lapar[49]	2014	USA	CABG, valvular, combination	49264	18.8	69 / 63	28.9 / 28.9	* / -	* / -	—
Lee[50]	2014	South Korea	Isolated CABG	1171	20.8	67 / 63	25.0 / 30.1	* / -	* / -	—
Lotfi[1]	2011	USA	Isolated CABG	3068	38.4	70 / 64	28.9 / 29.2	* / -	- / -	—
Mariscalco[10]	2014	UK, Italy	CABG, valvular, combination	17262	26.4	70 / 65	27.9 / 23.8	* / -	- / -	—
Nisanolgu[51]	2007	Turkey	Isolated CABG	426	21.4	71 / 70	27.5 / 31.3	* / -	- / -	—
O'Neal[52]	2013	USA	Isolated CABG	13165	22.1	68 / 62	27.0 / 30.0	* / -	- / -	—
Philip[53]	2014	USA	Isolated CABG	5135	29.0	68 / 63	27.2 / 29.0	* / *	- / -	1

Continued

Table 1. Continued.

Author	Year	Country	Surgery type	N	POAF (% incidence)	Age (POAF / no POAF)	Female sex (%) (POAF / no POAF)	Stroke outcomes (short-term / long-term)	Multivariable adjusted r esults (short-term / long-term)	Follow-up (years)
Pivatto Junior[54]	2014	Brazil	Isolated AVR	348	32.8	77 / 77	48.2 / 41.9	* / -	- / -	—
Rubin[55]	1987	USA	Isolated CABG	123	29.3	59 / 54	—	* / *	- / -	2.2
Saxena[56]	2012	Australia	Isolated CABG	19497	28.5	69 / 64	—	* / -	* / -	—
Shen[57]	2011	USA	CABG, valvular, combination, other	10390	30.2	—	35.7 / 35.0	* / -	- / -	—
Silva[58]	2004	Brazil	CABG, valvular, combination	158	28.5	-	37.8 / 35.4	* / -	- / -	-
Stamou[59]	2000	USA	Isolated CABG (off-pump)	969	21.3	69 / 61	33.5 / 33.4	* / -	- / -	-
Swinkels[60]	2017	The Netherlands	Isolated AVR	569	42.4	65 / 64	44.4 / 43.6	* / *	- / -	17.8
Thoren[13]	2020	Sweden	Isolated CABG	7145	30.6	69 / 65	21.0 / 23.0	- / *	- / *	9.8
Thoren[11]	2014	Sweden	Isolated CABG	6821	31.6	69 / 65	21.0 / 23.0	* / -	- / -	-
Villareal[61]	2004	USA	Isolated CABG	6475	15.4	68 / 62	26.7 / 26.1	* / -	* / -	-
Vlahou[62]	2016	Greece	Isolated CABG	446	24.9	68 / 64	16.2 / 14.6	* / -	- / -	-
Vural[63]	2019	Turkey	Isolated CABG	756	21.3	-	32.3 / 29.7	* / -	- / -	-
Whitlock[2]	2014	Canada	CABG, valvular, combination	99137	18.2	-	26.4 / 24.9	* / *	* / *	2
Yokota[64]	2017	Japan	Valvular ± other	119	39.5	76 / 71	48.9 / 45.8	* / -	- / -	-
Zangrillo[65]	2004	Italy	Isolated CABG	160	20.6	68 / 64	12.1 / 15.7	* / -	- / -	-
Zhao[66]	2015	Singapore	CABG ± valvular	160	22.6	62	14.3	* / -	- / -	-

Outcome (-): outcome not reported. Outcome (*): outcome reported. Multivariable adjustment (-): no data or adjustment results not used in meta-analysis. Multivariable adjustment (*): multivariable adjusted results used in meta-analysis.

AVR, aortic valve replacement and/or repair; CABG, coronary artery bypass surgery; LVAD, left ventricular assist device; MVR, mitral valve replacement and/or repair; POAF, perioperative atrial fibrillation; TVR, tricuspid valve replacement and/or repair.

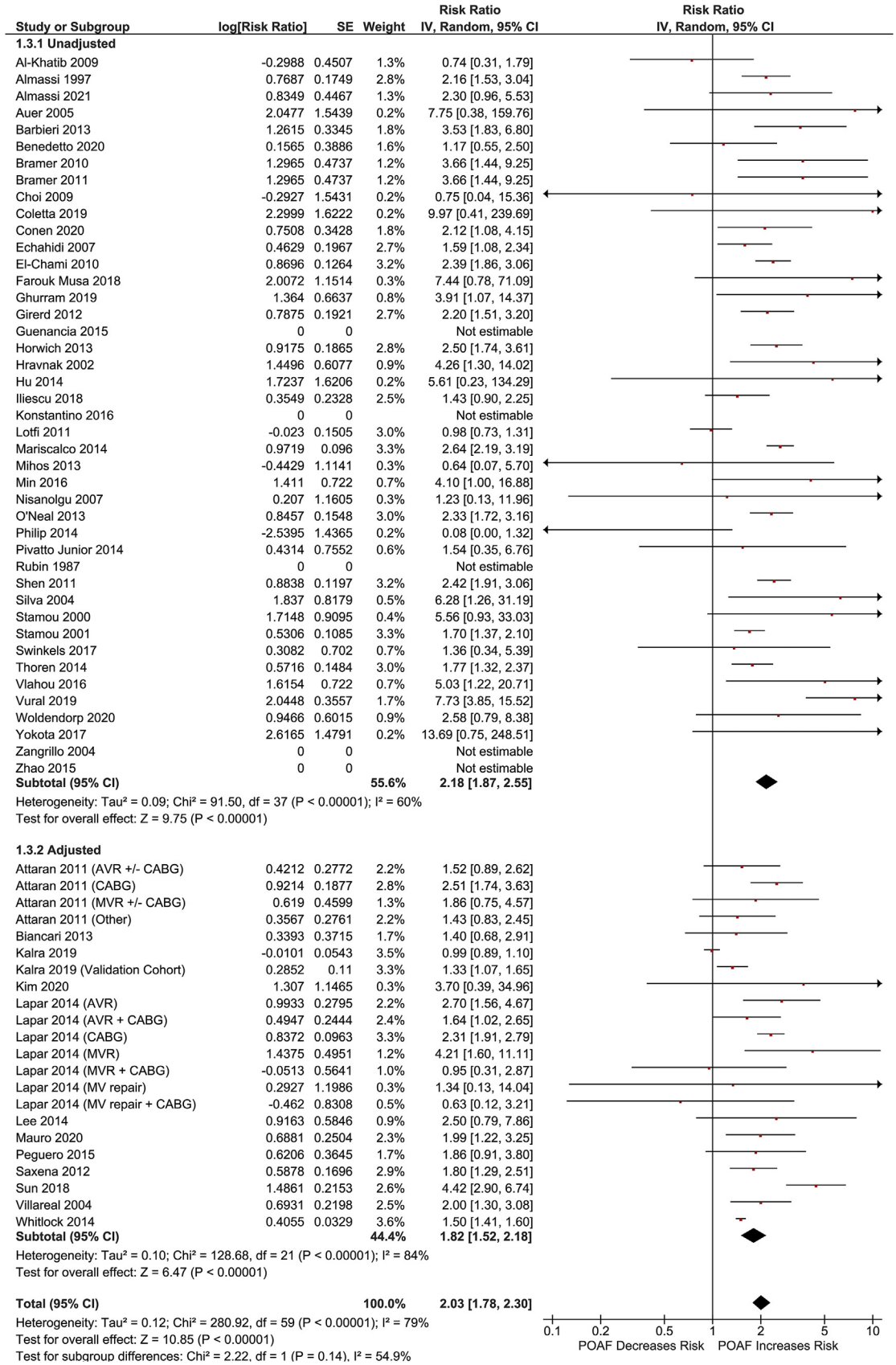

Figure 2. Forest plot for short-term risk of stroke. Forest plot for short-term stroke risk in patients with vs without perioperative atrial fibrillation (POAF), stratified by studies with vs without multivariable adjustment. Results are reported as an overall risk ratio. Short-term stroke is defined as in-hospital events or events occurring within 30 days of surgery. AVR, aortic valve replacement; CABG, coronary artery bypass graft; df, degrees of freedom; IV, inverse variance; MV, mitral valve; MVR, mitral valve replacement; SE, standard error.

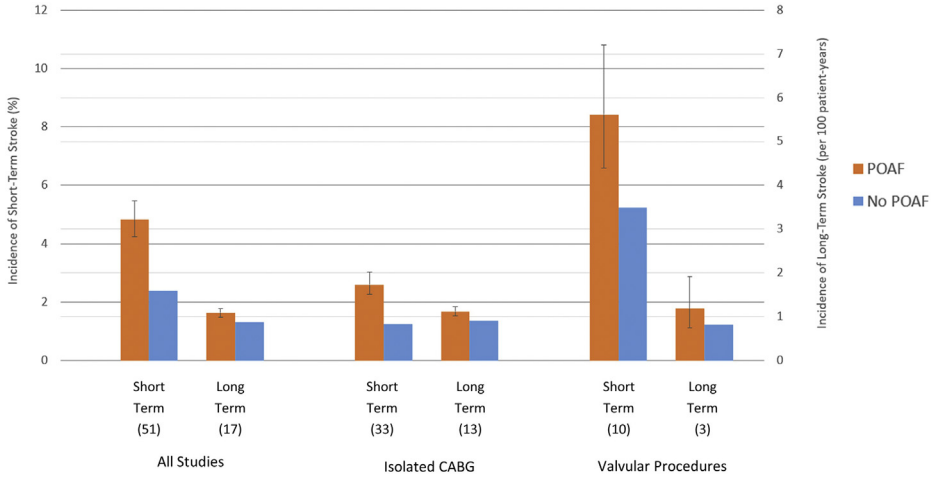

Figure 3. Estimated absolute risks for short-term and long-term stroke. Estimated absolute risks of short-term and long-term stroke stratified by perioperative atrial fibrillation (POAF) status and type of surgery. The number of included studies used to estimate the baseline risk is indicated in brackets. Absolute risks are estimated in the POAF group using the relative risks calculated from the study meta-analyses. **Error bars** represent 95% confidence intervals (CIs).

Sensitivity analyses of high-quality studies, studies reporting only ischemic or embolic strokes, studies published in the year 2010 or later, and studies that specified the method by which POAF was detected demonstrated consistent results (Supplemental Table S6).

Discussion

In this systematic review and meta-analysis of 55 studies with over 500,000 participants undergoing cardiac surgery, we found that POAF was associated with an increased risk of short-term and long-term stroke. Patients with POAF had a 2% higher absolute risk of short-term stroke, compared to patients without POAF. In contrast, the absolute risk of stroke was only 0.18 per 100 patient-years higher in patients with POAF during long-term follow-up. These differences in risk suggest that short-term and long-term stroke prevention in POAF patients should be approached separately.

Although anticoagulation is the cornerstone of stroke prevention in patients with chronic nonoperative AF, its routine use in patients with POAF after cardiac surgery is controversial. Although guidelines suggest that clinicians should consider anticoagulation in this scenario,[67,68] no high-quality evidence supports these recommendations. Some groups have recommended a limited treatment duration of 4 weeks after sinus rhythm restoration.[69] Our meta-analysis found that the increased risk of stroke with POAF was concentrated in the early postoperative period, suggesting that such a strategy may be beneficial.

In the absence of high-quality data, however, there are several important knowledge gaps associated with such an approach. First, many short-term strokes occur during or shortly after surgery, and therefore cannot be prevented with anticoagulation therapy. A retrospective cohort study by Kollar et al. that included 2964 patients undergoing CABG found that 4 of 9 early strokes occurred intraoperatively.[70] Intraoperative strokes are thought to be common during valvular surgeries also.[71] In our meta-analysis, we found that patients with POAF undergoing valvular procedures had a higher absolute risk increase in short-term stroke than those undergoing isolated CABG surgery. A plausible possibility is that intraoperative factors specific to valvular procedures, such as longer cross-clamping times and embolization risk during surgical excision,[71,72] contributed to the higher stroke risk. Second, alternate pathophysiologic mechanisms may mediate the short-term risk of postoperative stroke in POAF, for which the effectiveness of anticoagulation is uncertain. Kollar et al. found that 2 of the 4 postoperative strokes occurring after POAF were caused by atherosclerotic disease in the carotid and vertebral arteries.[70] Third, excess bleeding from early anticoagulation use may outweigh any potential reduction in stroke. A retrospective study of 166,747 post-CABG patients with POAF found that anticoagulation use on discharge was associated with a significant increase in re-hospitalization rates for major bleeding at 30 days after surgery (0.98% vs 0.23%; adjusted odds ratio 4.30; 95% CI, 3.69-5.03) without a reduction in hospitalizations for stroke.[73] The results of an ongoing clinical trial randomizing patients to either warfarin or standard antiplatelet therapy for 3 months after CABG will inform clinicians on the best management strategy for preventing short-term strokes.[74] Until these results become available, short-term use of anticoagulation remains an unproven strategy.

It has been hypothesized that POAF may represent the first manifestation of sustained AF, and that long-term strokes may be caused by subsequent AF recurrences.[7] However, several key differences between POAF and nonoperative AF suggest that the 2 may be separate entities. First, many patients with POAF do not have documented AF recurrence. One randomized controlled trial of cardiac surgery patients with POAF found that less than 5% of participants had clinical evidence of AF at their 2-month follow-up visit.[5] Second, our meta-analysis found that the estimated long-term stroke risk in patients with POAF was low (1.06 events per

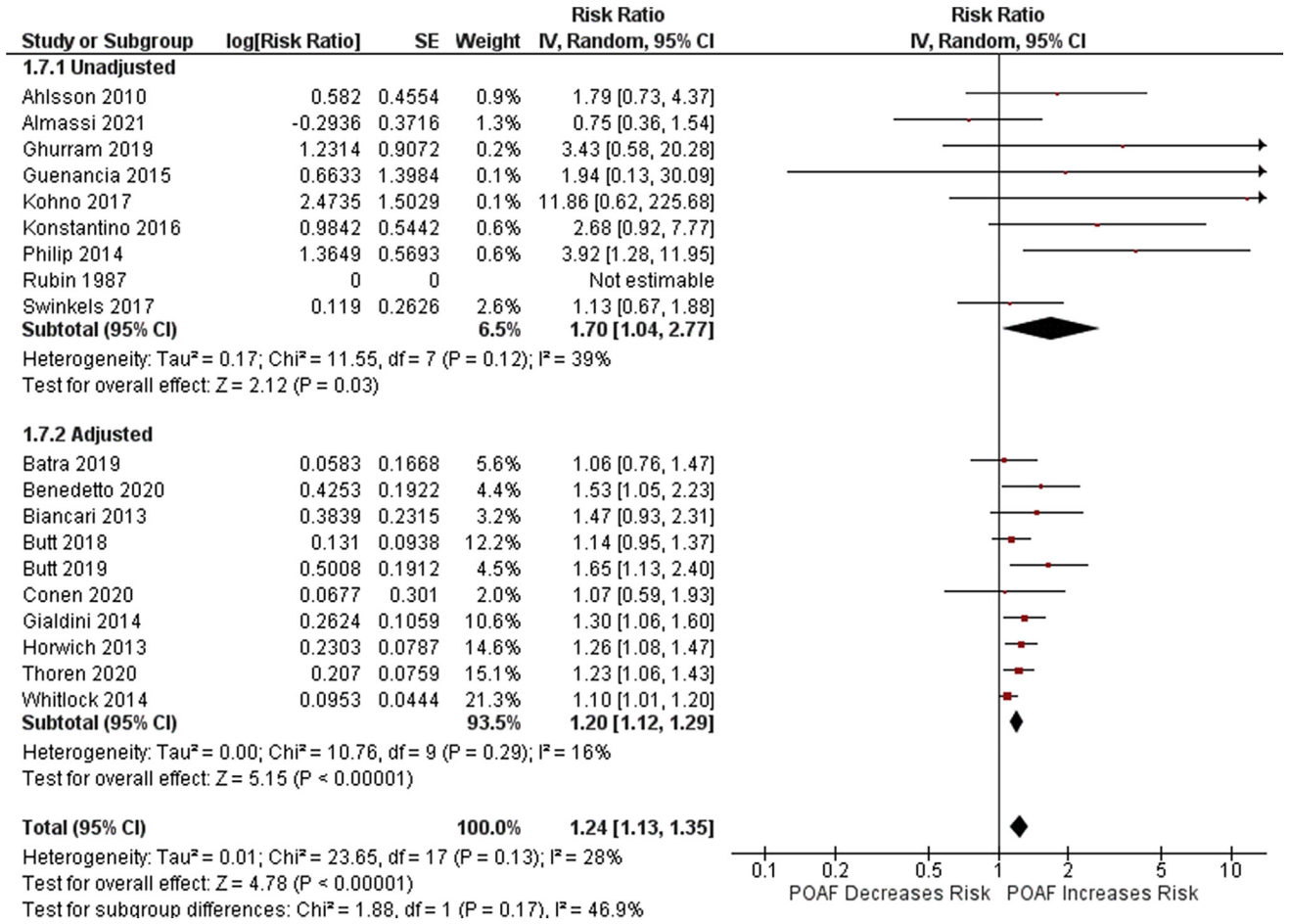

Figure 4. Forest plot for long-term risk of stroke. Forest plot for long-term stroke risk in patients with vs without perioperative atrial fibrillation (POAF), stratified by studies with vs without multivariable adjustment. Results are reported as an overall risk ratio. Long-term stroke is defined as strokes occurring > 30 days after surgery or after hospital discharge. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error.

100 patient-years). For patients with nonoperative AF who are at a similar stroke risk, there is no universal recommendation for anticoagulation use.[67,68,75] Third, given that the long-term difference in stroke risk was very small (0.18 per 100 patient-years) between patients with vs without POAF, the benefit of long-term anticoagulation in POAF patients is likely small. This is apparent when the risk increase is compared to that seen with other stroke risk factors. For example, the presence of asymptomatic carotid stenosis (60% or greater) conveys a much larger absolute risk increase of 2.3% per year for long-term stroke.[76] Finally, even if anticoagulation were an effective therapy for reducing stroke, the risks of bleeding need to be considered. For instance, in a registry study of 7368 cardiac surgery patients with POAF, use of anticoagulation led to more bleeding events (adjusted HR 1.4; 95% CI, 1.08-1.81), with no long-term differences in thromboembolism.[77]

Therefore, until better evidence is available, anticoagulation cannot be universally recommended in patients with POAF after cardiac surgery. However, our data suggest that it would be difficult to show a net clinical benefit for all POAF patients in a randomized controlled trial of long-term anticoagulation. A benefit may nevertheless be achievable in higher-risk subgroups. Our post hoc analysis suggests that patients with POAF and a prior history of stroke have a higher absolute risk of subsequent stroke, providing a potential target population for a future anticoagulation trial in patients with POAF after cardiac surgery.

The current systematic review and meta-analysis provides significant methodological improvements over previous publications. First, we included all types of cardiac surgeries. Second, we strictly separated the analyses for short-term and long-term risks of stroke. Third, we obtained additional unpublished data. Fourth, we used more-stringent eligibility criteria compared to previous meta-analyses.[78-80] POAF had to be described as new in onset and reported independently from other tachyarrhythmias, and individual studies were not eligible if they omitted transient AF events or nonfatal strokes.

Our systematic review has limitations. A high degree of heterogeneity was detected among individual studies reporting short-term risk of stroke. Therefore, cautious interpretation of the summary estimate is warranted. Most studies reporting short-term stroke did not confirm whether strokes occurred after the onset of POAF, limiting the establishment of causality. However, the vast majority of long-term studies clearly specified that POAF occurred prior to stroke occurrence. Publication bias was detected in the analysis for long-term risk

of stroke, suggesting that small studies demonstrating no association or an inverse association of POAF with stroke may not be published. Nevertheless, our results remained robust after replacing these studies using the trim-and-fill method. Postoperative anticoagulation use may have lowered the observed magnitude of association between POAF and stroke. This lowering is unlikely to have had a significant effect on the overall risk estimates, given that the reported rates of anticoagulation use were generally low. However, there may be certain subgroups of patients, such as those with persistent or recurrent AF, who may still benefit from anticoagulation. As our study did not assess the duration of AF, we could not determine its effect on stroke risk.

Conclusion

In this systematic review and meta-analysis, POAF after cardiac surgery was associated with an increased risk of short-term and long-term stroke. Although a potentially relevant ARD in short-term stroke was observed, the role of early anticoagulation use in this setting remains unknown and is currently being investigated in clinical trials. Given the small ARD in long-term stroke for patients with vs without POAF, it is uncertain whether POAF patients benefit from long-term anticoagulation therapy.

Funding Sources

The authors have no sources of funding to declare.

Disclosures

Dr Devereaux has received grants from Abbott Diagnostics, Boehringer Ingelheim, Philips Healthcare, Roche Diagnostics, and Siemens, outside the submitted work. Dr Devereaux has participated in advisory board meetings for Boehringer Ingelheim, Bayer, and Quidel Canada, and has attended an expert panel meeting with Boehringer Ingelheim, outside the submitted work. Dr Whitlock has received grants from Bayer, Roche, and Boehringer Ingelheim, and consultancy fees from PhaseBio, Atricure, and Boehringer Ingelheim, outside the submitted work. Dr Healey has received grants and speaking fees from BMS/Pfizer and Servier, outside the submitted work. Dr McIntyre has received speaking fees from Bayer and Servier, outside the submitted work. Dr Belley-Côté has received grants from Bayer and Roche, outside the submitted work. Dr Conen has received consultancy fees from Servier Canada, and Roche Diagnostics, outside the submitted work. All the other authors have no conflicts of interest to disclose.

References

1. Lotfi A, Wartak S, Sethi P, Garb J, Giugliano GR. Postoperative atrial fibrillation is not associated with an increased risk of stroke or the type and number of grafts: a single-center retrospective analysis. Clin Cardiol 2011;34:787-90.
2. Whitlock R, Healey JS, Connolly SJ, et al. Predictors of early and late stroke following cardiac surgery. CMAJ 2014;186:905-11.
3. Butt JH, Olesen JB, Gundlund A, et al. Long-term thromboembolic risk in patients with postoperative atrial fibrillation after left-sided heart valve surgery. JAMA Cardiol 2019;4:1139-47.
4. Zakkar M, Ascione R, James AF, Angelini GD, Suleiman MS. Inflammation, oxidative stress and postoperative atrial fibrillation in cardiac surgery. Pharmacol Ther 2015;154:13-20.
5. Gillinov AM, Bagiella E, Moskowitz AJ, et al. Rate control versus rhythm control for atrial fibrillation after cardiac surgery. N Engl J Med 2016;374:1911-21.
6. Bessissow A, Khan J, Devereaux PJ, Alvarez-Garcia J, Alonso-Coello P. Postoperative atrial fibrillation in non-cardiac and cardiac surgery: an overview. J Thromb Haemost 2015;13(Suppl 1):S304-12.
7. El-Chami MF, Merchant FM, Smith P, et al. Management of new-onset postoperative atrial fibrillation utilizing insertable cardiac monitor technology to observe recurrence of AF (MONITOR-AF). Pacing Clin Electrophysiol 2016;39:1083-9.
8. Riad FS, German K, Deitz S, et al. Attitudes toward anticoagulation for postoperative atrial fibrillation: a nationwide survey of VA providers. Pacing Clin Electrophysiol 2020;43:1295-301.
9. El-Chami MF, Kilgo P, Thourani V, et al. New-onset atrial fibrillation predicts long-term mortality after coronary artery bypass graft. J Am Coll Cardiol 2010;55:1370-6.
10. Mariscalco G, Biancari F, Zanobini M, et al. Bedside tool for predicting the risk of postoperative atrial fibrillation after cardiac surgery: the POAF score. J Am Heart Assoc 2014;3:e000752.
11. Thorén E, Hellgren L, Granath F, Hörte LG, Ståhle E. Postoperative atrial fibrillation predicts cause-specific late mortality after coronary surgery. Scand Cardiovasc J 2014;48:71-8.
12. Butt JH, Xian Y, Peterson ED, et al. Long-term thromboembolic risk in patients with postoperative atrial fibrillation after coronary artery bypass graft surgery and patients with nonvalvular atrial fibrillation. JAMA Cardiol 2018;3:417-24.
13. Thorén E, Wernroth ML, Christersson C, et al. Compared with matched controls, patients with postoperative atrial fibrillation (POAF) have increased long-term AF after CABG, and POAF is further associated with increased ischemic stroke, heart failure and mortality even after adjustment for AF. Clin Res Cardiol 2020;109:1232-42.
14. Conen D, Wang MK, Devereaux PJ, et al. New-onset perioperative atrial fibrillation after coronary artery bypass grafting and long-term risk of adverse events: an analysis from the coronary trial. Observational Study 2021;10:e020426.
15. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-12.
16. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed March 9, 2021.
17. Deeks J, Higgins J, Altman D. Analysing data and undertaking meta-analyses. In: Cochrane Handbook for Systematic Reviews of Interventions. Vol 2020. Cochrane: 2019. Available at: https://training.cochrane.org/handbook. Accessed December 8, 2021.
18. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-34.
19. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:455-63.
20. Schünemann HJ, Viste GE, Higgings JPT, et al. Interpreting results and drawing conclusions. In: Higgins JPT, Santesso N, Deesk JJ, Glasziou P,

eds. Cochrane Handbook for Systematic Reviews of Interventions. city: Cochrane; 2020. Available at: www.training.cochrane.org/handbook. Accessed December 8, 2021.

21. Ahlsson A, Fengsrud E, Bodin L, Englund A. Postoperative atrial fibrillation in patients undergoing aortocoronary bypass surgery carries an eightfold risk of future atrial fibrillation and a doubled cardiovascular mortality. Eur J Cardiothorac Surg 2010;37:1353-9.

22. Al-Khatib SM, Hafley G, Harrington RA, et al. Patterns of management of atrial fibrillation complicating coronary artery bypass grafting: results from the PRoject of Ex-vivo Vein graft ENgineering via Transfection IV (PREVENT-IV) Trial. Am Heart J 2009;158:792-8.

23. Almassi GH, Hawkins RB, Bishawi M, et al. New-onset postoperative atrial fibrillation impact on 5-year clinical outcomes and costs. J Thorac Cardiovasc Surg 2021;161:1803-10.

24. Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? Ann Surg 1997;226. 501-11; discussion 511—513.

25. Attaran S, Shaw M, Bond L, Pullan MD, Fabri BM. Atrial fibrillation postcardiac surgery: a common but a morbid complication. Interact Cardiovasc Thorac Surg 2011;12:772-7.

26. Auer J, Weber T, Berent R, et al. Risk factors of postoperative atrial fibrillation after cardiac surgery. J Card Surg 2005;20:425-31.

27. Barbieri LR, Sobral ML, Gerônimo GM, et al. Incidence of stroke and acute renal failure in patients of postoperative atrial fibrillation after myocardial revascularization. Rev Bras Cir Cardiovasc 2013;28:442-8.

28. Batra G, Ahlsson A, Lindahl B, et al. Atrial fibrillation in patients undergoing coronary artery surgery is associated with adverse outcome. Ups J Med Sci 2019;124:70-7.

29. Benedetto U, Gaudino MF, Dimagli A, et al. Postoperative atrial fibrillation and long-term risk of stroke after isolated coronary artery bypass graft surgery. Circulation 2020;142:1320-9.

30. Biancari F, Asim Mahar MA, Kangasniemi OP. CHADS2 and CHA2DS2-VASc scores for prediction of immediate and late stroke after coronary artery bypass graft surgery. J Stroke Cerebrovasc Dis 2013;22: 1304-11.

31. Bramer S, van Straten AH, Soliman Hamad MA, et al. The impact of new-onset postoperative atrial fibrillation on mortality after coronary artery bypass grafting. Ann Thorac Surg 2010;90:443-9.

32. Bramer S, van Straten AH, Soliman Hamad MA, et al. New-onset postoperative atrial fibrillation predicts late mortality after mitral valve surgery. Ann Thorac Surg 2011;92:2091-6.

33. Choi YS, Shim JK, Hong SW, et al. Risk factors of atrial fibrillation following off-pump coronary artery bypass graft surgery: predictive value of C-reactive protein and transfusion requirement. Eur J Cardiothorac Surg 2009;36:838-43.

34. Coletta MJ, Lis G, Clark P, Dabir R, Daneshvar F. Reducing new-onset atrial fibrillation after coronary artery bypass graft surgery. AACN Adv Crit Care 2019;30:249-58.

35. Echahidi N, Mohty D, Pibarot P, et al. Obesity and metabolic syndrome are independent risk factors for atrial fibrillation after coronary artery bypass graft surgery. Circulation 2007;116:I213-9.

36. Farouk Musa A, Quan CZ, Xin LZ, et al. A retrospective study on atrial fibrillation after coronary artery bypass grafting surgery at The National Heart Institute, Kuala Lumpur. F1000Res 2018;7:164.

37. Gialdini G, Nearing K, Bhave PD, et al. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. JAMA 2014;312:616-22.

38. Ghurram A, Krishna N, Bhaskaran R, et al. Patients who develop postoperative atrial fibrillation have reduced survival after off-pump coronary artery bypass grafting. Indian J Thorac Cardiovasc Surg 2019;36:6-13.

39. Girerd N, Pibarot P, Daleau P, et al. Statins reduce short- and long-term mortality associated with postoperative atrial fibrillation after coronary artery bypass grafting: impact of postoperative atrial fibrillation and statin therapy on survival. Clin Cardiol 2012;35:430-6.

40. Guenancia C, Pujos C, Debomy F, et al. Incidence and predictors of new-onset silent atrial fibrillation after coronary artery bypass graft surgery. Biomed Res Int 2015;2015:703685.

41. Horwich P, Buth KJ, Légaré JF. New onset postoperative atrial fibrillation is associated with a long-term risk for stroke and death following cardiac surgery. J Card Surg 2013;28:8-13.

42. Hravnak M, Hoffman LA, Saul MI, et al. Predictors and impact of atrial fibrillation after isolated coronary artery bypass grafting. Crit Care Med 2002;30:330-7.

43. Hu J, Peng L, Qian H, et al. Transoesophageal echocardiography for prediction of postoperative atrial fibrillation after isolated aortic valve replacement: two-dimensional speckle tracking for intraoperative assessment of left ventricular longitudinal strain. Eur J Cardiothorac Surg 2015;47:833-9.

44. Iliescu AC, Salaru DL, Achitei I, et al. Postoperative atrial fibrillation prediction following isolated surgical aortic valve replacement. Anatol J Cardiol 2018;19:394-400.

45. Kalra R, Patel N, Doshi R, Arora G, Arora P. Evaluation of the incidence of new-onset atrial fibrillation after aortic valve replacement. JAMA Intern Med 2019;179:1122-30.

46. Kim SH, Hwang HY, Choi JW, et al. The impact of beta-blocker use on postoperative atrial fibrillation after aortic valve replacement. J Thorac Dis 2020;12:2545-52.

47. Kohno H, Ueda H, Matsuura K, et al. Long-term consequences of atrial fibrillation after aortic valve replacement. Asian Cardiovasc Thorac Ann 2017;25:179-91.

48. Konstantino Y, Zelnik Yovel D, et al. Postoperative atrial fibrillation following coronary artery bypass graft surgery predicts long-term atrial fibrillation and stroke. Isr Med Assoc J 2016;18:744-8.

49. LaPar DJ, Speir AM, Crosby IK, et al. Postoperative atrial fibrillation significantly increases mortality, hospital readmission, and hospital costs. Ann Thorac Surg 2014;98:527-33. discussion 533.

50. Lee SH, Kang DR, Uhm JS, et al. New-onset atrial fibrillation predicts long-term newly developed atrial fibrillation after coronary artery bypass graft. Am Heart J 2014;167:593-600.e591.

51. Nisanoglu V, Erdil N, Aldemir M, et al. Atrial fibrillation after coronary artery bypass grafting in elderly patients: incidence and risk factor analysis. Thorac Cardiovasc Surg 2007;55:32-8.

52. O'Neal WT, Efird JT, Davies SW, et al. Impact of race and postoperative atrial fibrillation on long-term survival after coronary artery bypass grafting. J Card Surg 2013;28:484-91.

53. Philip F, Becker M, Galla J, Blackstone E, Kapadia SR. Transient postoperative atrial fibrillation predicts short and long term adverse events following CABG. Cardiovasc Diagn Ther 2014;4:365-72.

54. Pivatto Júnior F, Teixeira Filho GF, Sant'anna JR, et al. Advanced age and incidence of atrial fibrillation in the postoperative period of aortic valve replacement. Rev Bras Cir Cardiovasc 2014;29:45-50.

55. Rubin DA, Nieminski KE, Reed GE, Herman MV. Predictors, prevention, and long-term prognosis of atrial fibrillation after coronary

artery bypass graft operations. J Thorac Cardiovasc Surg 1987;94:331-5.

56. Saxena A, Dinh DT, Smith JA, et al. Usefulness of postoperative atrial fibrillation as an independent predictor for worse early and late outcomes after isolated coronary artery bypass grafting (multicenter Australian study of 19,497 patients). Am J Cardiol 2012;109:219-25.

57. Shen J, Lall S, Zheng V, et al. The persistent problem of new-onset postoperative atrial fibrillation: a single-institution experience over two decades. J Thorac Cardiovasc Surg 2011;141:559-70.

58. Silva RG, Lima GG, Laranjeira A, et al. Risk factors, morbidity, and mortality associated with atrial fibrillation in the postoperative period of cardiac surgery. Arq Bras Cardiol 2004;83:105-10. 199-204.

59. Stamou SC, Dangas G, Hill PC, et al. Atrial fibrillation after beating heart surgery. Am J Cardiol 2000;86:64-7.

60. Swinkels BM, de Mol BA, Kelder JC, Vermeulen FE, Ten Berg JM. New-onset postoperative atrial fibrillation after aortic valve replacement: effect on long-term survival. J Thorac Cardiovasc Surg 2017;154:492-8.

61. Villareal RP, Hariharan R, Liu BC, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol 2004;43:742-8.

62. Vlahou A, Diplaris K, Ampatzidou F, Karagounnis L, Drossos G. The role of blood transfusion in the development of atrial fibrillation after coronary artery bypass grafting. Thorac Cardiovasc Surg 2016;64:688-92.

63. Vural Ü, Ağlar AA. What is the role of metabolic syndrome and obesity for postoperative atrial fibrillation after coronary bypass grafting? BMC Cardiovasc Disord 2019;19:147.

64. Yokota J, Nishi H, Sekiya N, Yamada M, Takahashi T. Atrial fibrillation following aortic valve replacement: impact of perioperative use of intravenous β-blocker. Gen Thorac Cardiovasc Surg 2017;65:194-9.

65. Zangrillo A, Landoni G, Sparicio D, et al. Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth 2004;18:704-8.

66. Zhao LP, Kofidis T, Lim TW, et al. Sleep apnea is associated with new-onset atrial fibrillation after coronary artery bypass grafting. J Crit Care 2015;30. 1418.e1411-15.

67. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J 2021;42:373-498.

68. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1-76.

69. Frendl G, Sodickson AC, Chung MK, et al. 2014 AATS guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures. J Thorac Cardiovasc Surg 2014;148:e153-93.

70. Kollar A, Lick SD, Vasquez KN, Conti VR. Relationship of atrial fibrillation and stroke after coronary artery bypass graft surgery: When is anticoagulation indicated? Ann Thorac Surg 2006;82:515-23.

71. Grabert S, Lange R, Bleiziffer S. Incidence and causes of silent and symptomatic stroke following surgical and transcatheter aortic valve replacement: a comprehensive review. Interact Cardiovasc Thorac Surg 2016;23:469-76.

72. Al-Sarraf N, Thalib L, Hughes A, et al. Cross-clamp time is an independent predictor of mortality and morbidity in low- and high-risk cardiac patients. Int J Surg 2011;9:104-9.

73. Matos JD, McIlvaine S, Grau-Sepulveda M, et al. Anticoagulation and amiodarone for new atrial fibrillation after coronary artery bypass grafting: prescription patterns and 30-day outcomes in the United States and Canada. J Thorac Cardiovasc Surg 2021;162:616-624.e3.

74. Anticoagulation for New-Onset Post-Operative Atrial Fibrillation After CABG (PACES). Available at: https://clinicaltrials.gov/ct2/show/NCT04045665. Accessed March 9, 2021.

75. Lip GYH, Frison L, Halperin JL, Lane DA. Identifying patients at high risk for stroke despite anticoagulation. Stroke 2010;41:2731-8.

76. Inzitari D, Eliasziw M, Gates P, et al. The causes and risk of stroke in patients with asymptomatic internal-carotid-artery stenosis. North American Symptomatic Carotid Endarterectomy Trial collaborators. N Engl J Med 2000;342:1693-700.

77. Taha A, Nielsen SJ, Bergfeldt L, et al. New-onset atrial fibrillation after coronary artery bypass grafting and long-term outcome: a population-based nationwide study from the SWEDEHEART Registry. J Am Heart Assoc 2021;10:e017966.

78. Eikelboom R, Sanjanwala R, Le ML, Yamashita MH, Arora RC. Postoperative atrial fibrillation after cardiac surgery: a systematic review and meta-analysis. Ann Thorac Surg 2021;111:544-54.

79. Lin MH, Kamel H, Singer DE, et al. Perioperative/postoperative atrial fibrillation and risk of subsequent stroke and/or mortality. Stroke 2019;50:1364-71.

80. Megens MR, Churilov L, Thijs V. New-onset atrial fibrillation after coronary artery bypass graft and long-term risk of stroke: a meta-analysis. J Am Heart Assoc 2017;6. e007558.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2021.09.011.