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REVIEW

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New-onset atrial fibrillation following coronary bypass surgery predicts long-term mortality: a systematic review and meta-analysis

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Summary

Atrial fibrillation (AF) is one of the most common postoperative complications following cardiac surgery. Recent evidence suggests that postoperative atrial fibrillation (POAF) may be more 'malignant' than previously thought, associated with follow-up mortality and morbidity. To evaluate the long-term survival of POAF versus new-onset POAF (No-POAF) cohorts following coronary bypass surgery, the current meta-analysis with reconstructed individual patient data was performed. Electronic searches were performed using six databases from their inception to August 2014. Relevant studies with long-term survival data presented for POAF versus No-POAF were identified. Data were extracted by two independent reviewers and analysed according to predefined clinical endpoints. The pooled hazard ratio (HR) significantly favoured higher survival in No-POAF over POAF (HR 1.28; 95% CI, 1.19–1.37; $I^2 = 96\%$; $P < 0.00001$). Individual patient data of 69 518 patients were available for inverted Kaplan–Meier survival curve analysis. Analysis of aggregate data using Kaplan–Meier curve methods for POAF versus No-POAF groups determined survival rates at the 1-year (95.7 vs 98%), 2-year (92.3 vs 95.4%), 3-year (88.7 vs 93.9%), 5-year (82.6 vs 89.4%) and 10-year (65.5 vs 75.3%) follow-up. Other complications including 30-day mortality, strokes, respiratory failure, pneumonia and hospitalization were significantly higher in the POAF group. New-onset AF following coronary bypass surgery is associated with significantly higher risk of mortality in short- and long-term follow-up. Current evidence suggests the need for stricter surveillance and monitoring of POAF following coronary bypass surgery.

Keywords: Coronary bypass • Atrial fibrillation • Outcomes • Meta-analysis

INTRODUCTION

Atrial fibrillation (AF) is one of the most common postoperative complications following cardiac surgery. This in turn translates into longer hospitalization, increased cost of hospitalization as well as association with thromboembolic events and mortality [1–3]. Despite new-onset postoperative atrial fibrillation (No-POAF) occurring in 20–40% of patients [4–6] following coronary artery bypass graft (CABG) surgery, the underlying mechanisms are not well established. However, it has been traditionally thought to be transient and benign to the patient [7].

Recent evidence suggests that POAF may be more 'malignant' than previously thought, associated with follow-up mortality and morbidity [6, 8–10]. Several studies have provided compelling data to demonstrate the link between POAF and short-term mortality [11–13]. However, association between POAF and long-term mortality is not established, with rates at long-term follow-up not well defined. Given the increasing number of elderly and high-risk patients undergoing cardiac surgery and CABG, there is a need to elucidate the long-term influence of POAF, given that there are already known associations with comorbidities including heart failure, stroke, prolonged hospital stay and cost [11]. To evaluate the long-term survival of POAF versus No-POAF cohorts, the current meta-analysis with reconstructed individual patient data was performed.

METHODS

Literature search strategy

Electronic searches were performed using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP Journal Club and Database of Abstracts of Review of Effectiveness from their date of inception to August 2014. To achieve the maximum sensitivity of the search strategy, we combined variants of the terms: ('atrial fibrillation' OR 'postoperative atrial fibrillation' OR 'POAF') AND ('cardiac surgery' OR 'bypass' OR 'coronary artery bypass graft' OR 'CABG') as either key words or MeSH terms. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies, assessed using the inclusion and exclusion criteria.

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Selection criteria

Eligible comparative studies for the present systematic review and meta-analysis included those in which patient cohorts comparing CABG patients with POAF versus CABG patients without No-POAF and presenting longer-term survival rates ≥1 year. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for quantitative assessment at each time interval. Reference lists were also hand-searched for further relevant studies. All publications were limited to those involving human subjects and in the English language. Abstracts, case reports, conference presentations, editorials, reviews and expert opinions were excluded.

Data extraction and critical appraisal

The primary outcome of interest was all-cause mortality and aggregate survival at follow-up. Other extracted data included baseline patient characteristics, number of patients enrolled, postoperative complications including 30-day mortality, strokes, respiratory failure, pneumonia, myocardial infarctions and length of stay. All Kaplan–Meier curves were recorded and later digitized for reconstruction of individual patient data for each study.

All data were extracted from article texts, tables and figures. Two investigators (Kevin Phana, Hakeem S.K. Ha) independently reviewed and assessed the quality of each retrieved article. Discrepancies between the reviewers were resolved by discussion and consensus. The final results were reviewed by the senior investigator (Tristan D. Yan).

Statistical analysis

Clinical outcomes were assessed using standard meta-analysis technique, with the relative risk (RR) used as a summary statistic. Both fixed- and random-effect models were tested and used to calculate the pooled RR or weighted mean differences for the surgical literature. Since similar results were obtained, only results of the random-effect model are presented. χ^2 tests were used to study heterogeneity between trials. I^2 statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values greater than 50% considered as substantial heterogeneity.

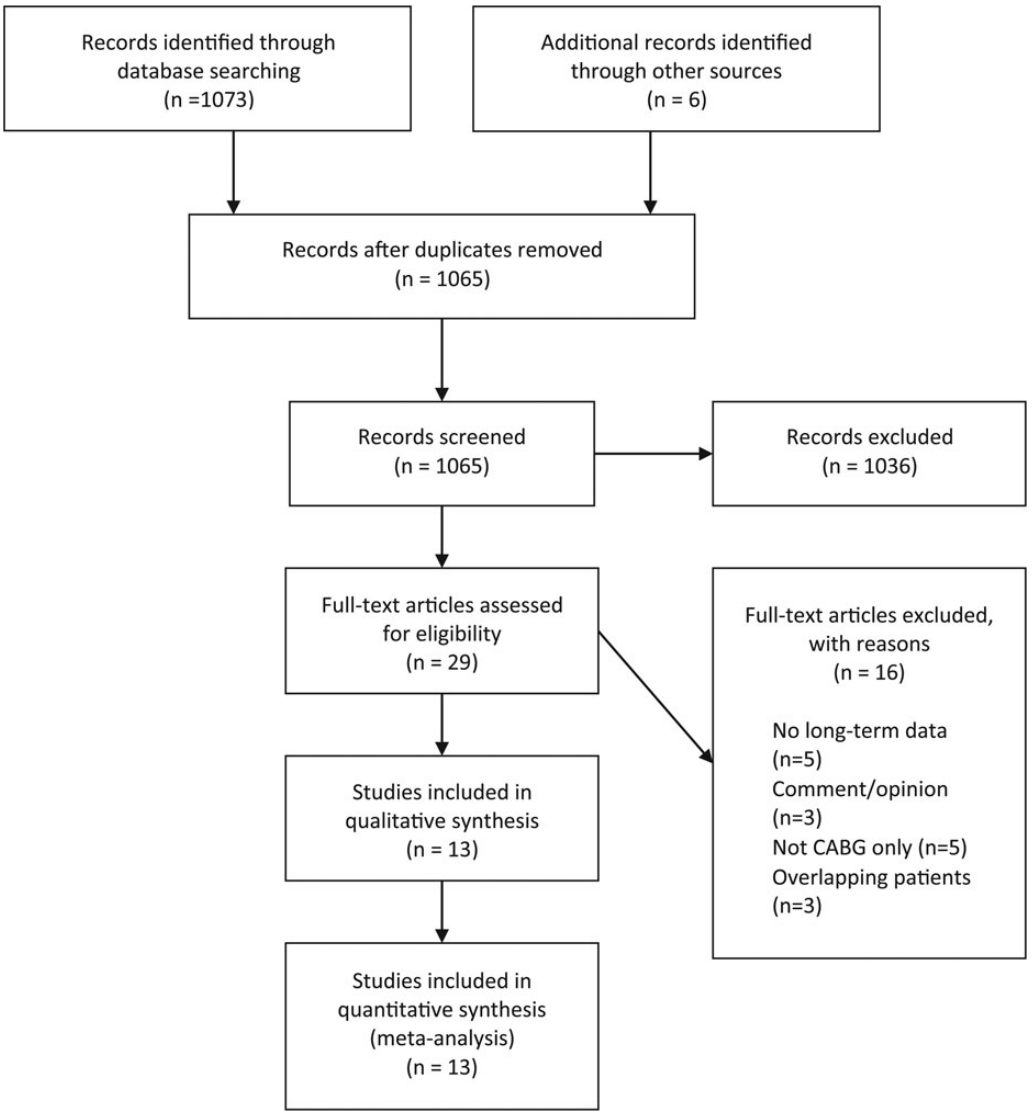

Figure 1: PRISMA flow chart of search strategy.

Individual patient survival data were reconstructed using an iterative algorithm that was applied to solve the Kaplan–Meier equations originally used to produce the published graphs. The mathematical basis of this algorithm is described in detail by Guyot *et al.* [14]. DigitizeIt software is used to digitize published Kaplan–Meier curves. This software essentially converts the published Kaplan–Meier curve into a set of coordinate points which accurately estimates all points on the graph. The digitized numerical data were used to solve numerical solutions to the inverted Kaplan–Meier equations as per algorithms in Guyot *et al.* The algorithm allowed the 'reconstruction' of patient-level data by estimating the 'alive' or 'dead' status of each patient on follow-up, which could then be aggregated to form combined survival curves for POAF and No-POAF cohorts. This algorithm assumes constant censoring and was calculated in R software (v.3.1.0).

Publication bias of the major outcomes of this meta-analysis was detected by Egger's regression test. If studies appeared to be missing in the areas of low statistical significance, then this indicates that there may be asymmetry due to publication bias. If studies appear to be missing in areas of high statistical significance, then publication bias is less likely a cause of funnel asymmetry.

All *P*-values were two-sided. All statistical analysis was conducted with Review Manager Version 5.2.1 (Cochrane Collaboration, Software Update, Oxford, UK), Comprehensive Meta-analysis v2.2 (Biostat, Inc., Englewood, USA) and R software version 2.1.

RESULTS

Quantity and quality of evidence

From the systematic literature search, a total of 1065 unique studies were identified. After exclusions of studies based on title and abstract screening, 29 studies remained for detailed analysis. Finally, 13 relevant studies [6, 9, 13, 15–24] were included in the present review of qualitative and quantitative analysis (Fig. 1).

All included studies were observational studies, including one prospective [23], three retrospective analyses of prospectively collected data [13, 15, 17] and nine retrospective observational studies [6, 9, 16, 18–22, 24]. There were 10 studies which recruited >1000 patients in each arm [9, 15, 17–24]. Thirty-day mortality was reported in 7 studies [6, 9, 13, 19–21, 23], whilst hazard ratios (HRs) for long-term survival was reported in 10 studies [9, 13, 15, 17–20, 22–24]. All included studies provided Kaplan–Meier curves for long-term survival actuarial survival rates. Study characteristics are summarized in Table 1.

Baseline and operation characteristics

The baseline patient and operation characteristics are summarized in Table 2. The weighted average age was significantly higher in the POAF cohort by 4.9 years (68.4 vs 63.5 years; $P < 0.00001$). The POAF group had a greater proportion of males (76.1 vs 73.9%; $P = 0.0001$). While the POAF group had fewer patients with hypertension (26.9 vs 68.1%; $P < 0.00001$), there were more individuals with prior strokes (10.2 vs 8.2%; $P < 0.00001$). Compared with No-POAF, POAF patients were more likely to have a background of heart failure (17.7 vs 13.2%; $P < 0.00001$), peripheral vascular disease (15.1 vs 11.9%; $P < 0.00001$), renal insufficiency (5 vs 4.3%; $P = 0.0009$) and chronic obstructive pulmonary disease (14.1 vs 11.7%; $P < 0.00001$). There was no difference between the POAF and No-POAF cohorts in terms of underlying prior myocardial infarcts, diabetes or high cholesterol. Use of beta-blockers and angiotensin-converting enzyme (ACE) inhibitors were also comparable between POAF and No-POAF cohorts.

In terms of operation parameters, no difference was found between POAF and No-POAF groups in terms of cardiopulmonary bypass duration (90.6 vs 87.9 min; $P = 0.12$) and cross-clamp duration (59.9 vs 57.3 min; $P = 0.08$). However, POAF was associated with significantly higher intra-aortic balloon pump (IABP) use (3.0 vs 1.6%; $P < 0.00001$) and higher inotrope use (27.4 vs 15.4%; $P < 0.00001$).

Table 1: Summary of study characteristics of new-onset postoperative atrial fibrillation after coronary artery bypass grafting

First author	Year	Study period	Institution	Country	Study type	*n* (POAF)	*n* (no AF)	Mean follow-up (years)
Thoren	2014	1996–2009	Uppsala University Hospital	Sweden	OS, R[a]	2152	4669	9.8 (0.1–17)[b]
Lee	2014	2005–09	Severance Cardiovascular Hospital, Yonsei University Health System	South Korea	OS, R	244	927	3.4 ± 1.9
Al-Shaar	2014	1994–2007	University of Toledo College of Medicine	USA	OS, R[a]	1211	5094	9.7 ± 4.2
O'Neal	2013	1992–2011	East Carolina Heart Institute	USA	OS, R	2907	10 258	8.2
Saxena	2012	2001–09	St Vincent's Hospital, Fitzroy	Australia	OS, R	5547	13 950	3.7 (0–8.8)[b]
Girerd	2012	2000–07	Quebec Heart Institute	Canada	OS, R	1868	4860	2.8
Attaran	2011	1998–2009	Liverpool Heart and Chest Hospital	UK	OS, R	3292	8843	NR
El-Chami	2010	1996–2007	Emory University Hospital/Emory Crawford Long Hospital	USA	OS, R	2985	13 184	6 (0–12)[b]
Bramer	2010	2003–07	Catharina Hospital	Netherlands	OS, P	1122	3976	2.5 (0–5.2)[b]
Ahlsson	2010	1999–2000	Orebro University Hospital	Sweden	OS, R[a]	165	406	6.9
Mariscalco	2009	1994–2004	Umea University Hospital	Sweden	OS, R	1748	5873	7.9
Filardo	2009	1997–2006	Baylor University Medical Centre	USA	OS, R	1814	5085	NR
Villareal	2004	1993–99	St Luke's Episcopal Hospital	USA	OS, R	994	5481	4 ± 2

POAF: postoperative atrial fibrillation; OS: observational study; R: retrospective; P: prospective; NR, not reported.
[a]Retrospective analysis of prospectively collected data.
[b]Range.

Table 2: Association between preoperative, intraoperative and postoperative variables and new-onset postoperative atrial fibrillation following coronary artery bypass grafting

Variable	No of studies	POAF	No-POAF	Associated effect (95% CI)	*P*-value	I^2	*P*-value for heterogeneity
Preoperative							
Age (years)	10	68.4 (*n* = 17 958)	63.5 (*n* = 55 494)	MD 4.90 (4.40–5.41)	<0.00001	90	<0.00001
Male	12	15 594/20 502 (76.1%)	50 771/68 656 (73.9%)	RR 1.02 (1.01–1.03)	0.0001	23	0.22
Hypertension	13	18 453/26 049 (26.9%)	55 726/81 818 (68.1%)	RR 1.05 (1.02–1.07)	<0.0001	84	<0.00001
Prior stroke	12	2431/23 897 (10.2%)	6415/77 937 (8.2%)	RR 1.26 (1.17–1.34)	<0.00001	45	0.04
Myocardial infarction	11	8193/23 179 (35.3%)	25 553/72 757 (35.1%)	RR 1.04 (0.99–1.09)	0.1	81	<0.00001
Heart failure	7	2783/15 702 (17.7%)	7135/53 979 (13.2%)	RR 1.33 (1.26–1.40)	<0.00001	32	0.19
PVD	10	3117/20 686 (15.1%)	8081/68 060 (11.9%)	RR 1.29 (1.16–1.44)	<0.00001	86	<0.00001
Diabetes mellitus	13	7519/26 049 (28.9%)	23 791/81 606 (29.2%)	RR 0.98 (0.94–1.03)	0.5	76	<0.00001
Renal insufficiency	9	1052/20 862 (5.0%)	2887/67 682 (4.3%)	RR 1.26 (1.10–1.44)	0.0009	71	0.0006
COPD	9	2632/18 626 (14.1%)	7472/63 603 (11.7%)	RR 1.27 (1.21–1.32)	<0.00001	10	0.35
Smoking	7	4103/13 368 (30.7%)	17 285/48 351 (35.7%)	RR 0.90 (0.82–0.99)	0.03	93	<0.00001
LVEF (%)	5	50.9 (*n* = 5599)	51.8 (*n* = 25 092)	MD 0.94 (−1.48, −0.40)	0.0007	36	0.18
Hypercholesterolaemia	5	9898/14 273 (69.3%)	30 656/47 479 (64.6%)	RR 0.95 (0.88–1.02)	0.19	56	0.04
Beta-blocker use	5	6540/9215 (71.0%)	25 029/34 323 (72.9%)	RR 1.02 (0.91–1.15)	0.71	98	<0.00001
ACEI use	3	2864/7760 (36.9%)	9612/28 302 (34.0%)	RR 1.05 (0.96–1.15)	0.27	87	0.0004
Intraoperative							
CPB time (min)	6	90.6 (*n* = 10 783)	87.9 (*n* = 31 110)	MD 2.47 (−0.67, 5.62)	0.12	94	<0.00001
Cross-clamp time (min)	5	59.9 (*n* = 9572)	57.3 (*n* = 26 016)	MD 2.60 (−0.28, 5.48)	0.08	95	<0.00001
IABP use	7	387/13 086 (3.0%)	668/42 768 (1.6%)	RR 1.74 (1.39–2.16)	<0.00001	60	0.02
Inotrope use	3	1712/6237 (27.4%)	2191/14 245 (15.4%)	RR 1.34 (1.27–1.41)	<0.00001	0	0.5
Postoperative							
30-day mortality	7	368/14 736 (2.5%)	634/43 389 (1.5%)	RR 1.95 (1.61–2.36)	<0.00001	45	0.09
Stroke	11	644/24 127 (2.7%)	991/75 186 (1.3%)	RR 2.06 (1.77–2.41)	<0.00001	52	0.02
Respiratory failure	4	565/8634 (6.5%)	1191/34 796 (3.4%)	RR 2.46 (1.77–3.41)	<0.00001	89	<0.00001
Pneumonia	5	626/11 972 (5.2%)	845/33 780 (2.5%)	RR 2.34 (1.75–3.14)	<0.00001	80	0.0005
Myocardial infarction	7	631/19 731 (3.2%)	1587/55 680 (2.9%)	RR 1.09 (0.87–1.37)	0.44	80	<0.0001
Length of stay (days)	4	11.0 (*n* = 7704)	8.9 (*n* = 21 156)	RR 2.14 (1.33–2.95)	<0.00001	90	<0.00001

POAF: postoperative atrial fibrillation; CI: confidence interval; RR: relative risk; MD: mean difference; PVD: peripheral vascular disease; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; ACEI: angiotensin-converting enzyme inhibitor; CPB: cardiopulmonary bypass; IABP: intra-aortic balloon pump.

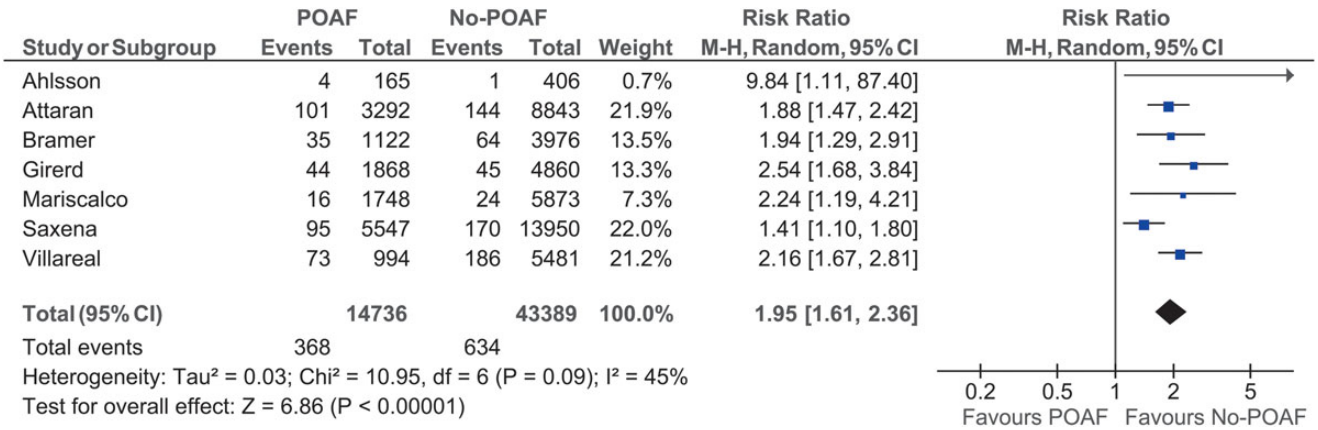

Figure 2: Forest plot of the 30-day mortality risk associated with new-onset postoperative atrial fibrillation (No-POAF) following coronary artery bypass grafting.

Assessment of postoperative complications

The 30-day mortality rate was significantly higher in the POAF cohort compared with No-POAF following CABG surgery (2.5 vs 1.5%; $P < 0.00001$; Fig. 2). Other complications were also significantly higher in the post-CABG AF group including strokes (2.7 vs 1.3%; $P < 0.00001$), respiratory failure (6.5 vs 3.4%; $P < 0.00001$), pneumonia (5.2 vs 2.5%; $P < 0.00001$) and longer hospitalization (11 vs 8.9 days; $P < 0.00001$). There was no difference between the cohorts for myocardial infarctions (3.2 vs 2.9%; $P = 0.44$) (Fig. 3).

Assessment of long-term survival

The overall adjusted HR from each included study was pooled to determine the overall long-term survival comparing POAF versus No-POAF groups. The pooled HR significantly favoured No-POAF

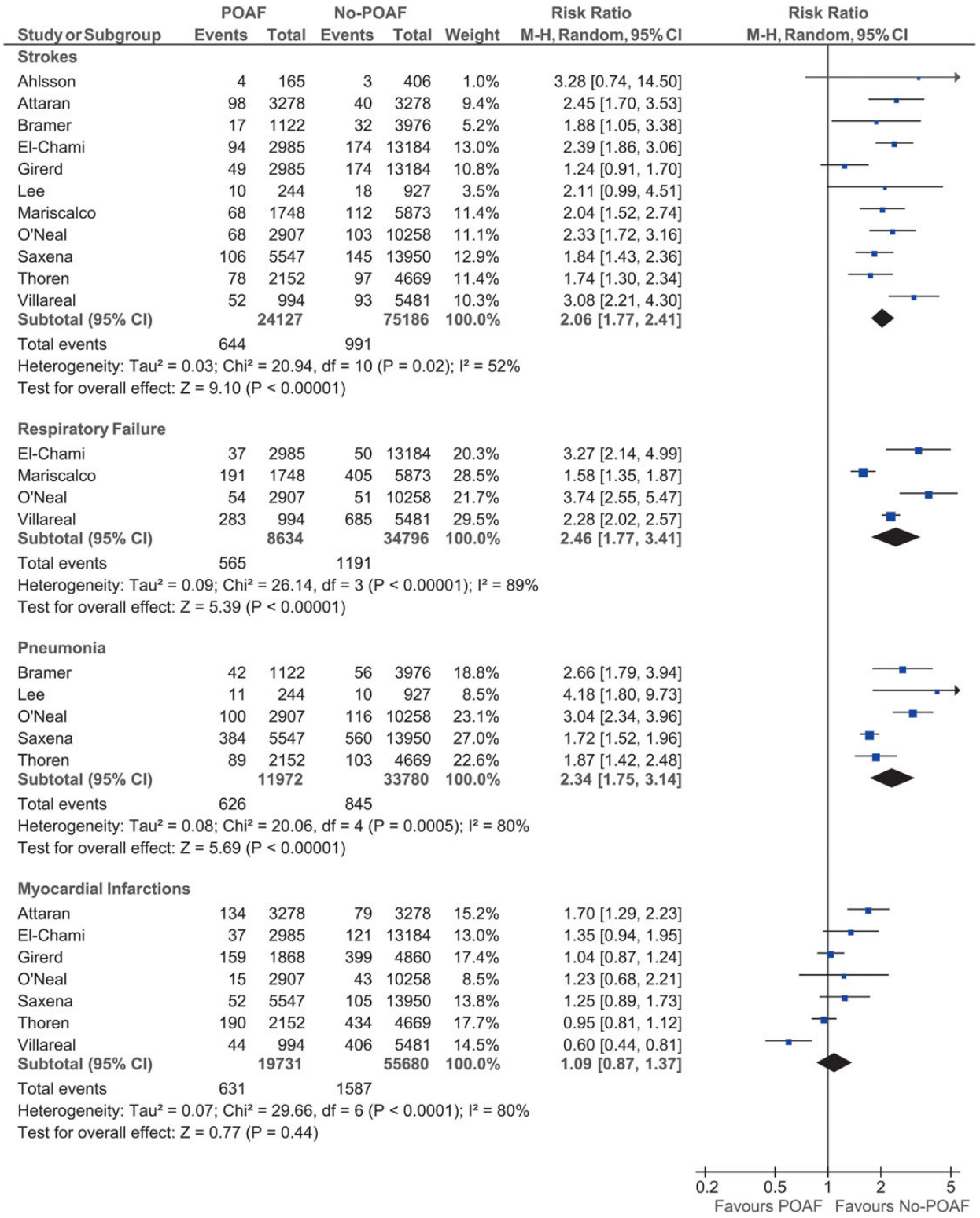

Figure 3: Forest plot of postoperative complications including strokes, respiratory failure, pneumonia, myocardial infarction, for bypass cohorts with postoperative atrial fibrillation (POAF) versus new-onset postoperative atrial fibrillation (No-POAF).

over POAF (HR 1.28; 95% CI, 1.19–1.37; $I^2 = 96\%$; $P < 0.00001$; Fig. 4).

Individual patient data of 69 518 patients were available for inverted Kaplan–Meier survival curve analysis. From this, 16 601 patients were from the POAF cohort and 52 917 patients were from the No-POAF cohort. Analysis of aggregate data using Kaplan–Meier curve methods for POAF versus No-POAF groups determined survival rates at the 1-year (95.7 vs 98%), 2-year (92.3 vs 95.4%), 3-year (88.7 vs 93.9%), 5-year (82.6 vs 89.4%) and 10-year (65.5 vs 75.3%) follow-up (Fig. 5).

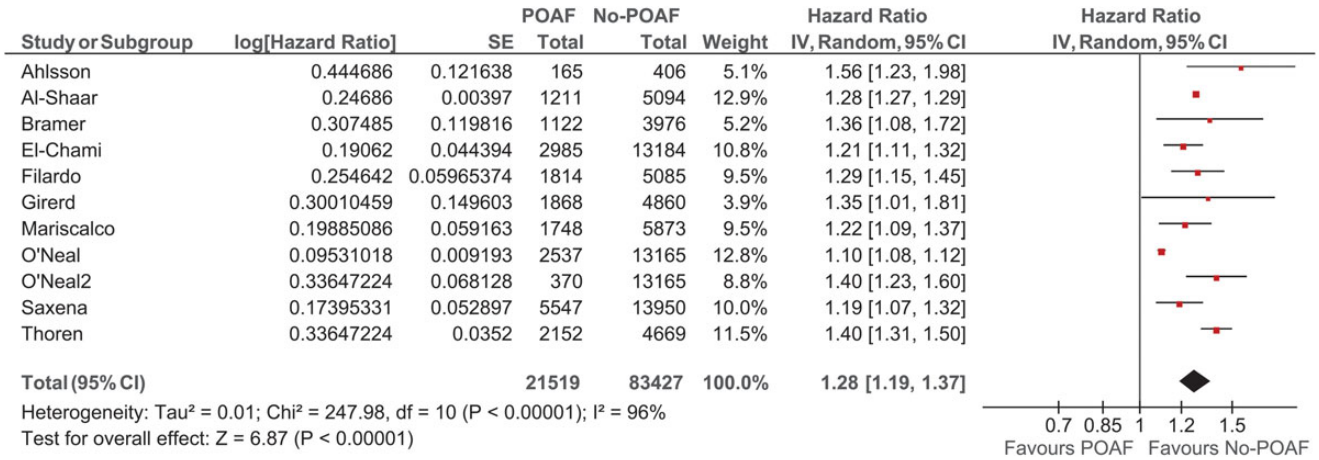

Figure 4: Forest plot of overall long-term mortality risk associated with new-onset postoperative atrial fibrillation (No-POAF) following coronary artery bypass grafting.

Publication bias

Begg's rank correlation method ($P = 0.640$) and Egger's weighted ($P = 0.884$) regression method were performed to assess publication bias in long-term mortality outcomes. Although both tests suggest that publication bias was not an influencing factor when mortality was selected as an outcome measure for all included studies, visual inspection of the funnel plot suggests a small study effect exists (Supplementary Fig. 1). Using the imputed trim and fill method, two studies were estimated to be 'missing', with the point estimate for mortality adjusted slightly from 1.276 (95% CI, 1.19–1.37) to 1.250 (95% CI, 1.17–1.33).

DISCUSSION

POAF was thought to be a well-tolerated, benign and self-limiting complication of cardiac surgery that was temporary and easily treated [7, 25, 26]. There is now slowly growing evidence that No-POAF may be associated with short-term and long-term mortality and morbidity following CABG [17, 22]. While there is consistent pooled evidence to show the efficacy of concomitant treatment of AF during cardiac surgery [27–31], the approach and management of No-POAF after cardiac surgery remains unclear.

In the present meta-analysis of 109 399 patients, significantly higher mortality was associated with new-onset POAF versus No-POAF, both in terms of 30-day and long-term follow-up. Pooled HRs and aggregated survival from reconstructed individual patient data suggested up to 10% higher actuarial survival in the No-POAF versus POAF cohort even at the 15-year follow-up. Significant higher complications including strokes, respiratory failure and longer hospitalization, as well as advanced age, were also found to be associated with POAF. Assessment of risk factors demonstrated that the POAF group had greater use of IABP and inotropes intraoperatively. No differences in preoperative ACE inhibitor use were found between POAF and No-POAF groups. It was also found that use was similar between POAF and No-POAF cohorts (71 vs 72.9%; $P = 0.71$). Overall, we believe that there is compelling evidence to warrant concern surrounding POAF and its association with long-term survival and morbidities [28]. Whether this association is causal or not cannot be answered by the present study. However, one potential explanation is that POAF is a surrogate marker for a more severe general status, which may translate to higher mortality rates over time.

The mechanisms responsible for No-POAF following CABG are still a matter of contentious debate, requiring further elucidation. There have been several explanations proposed to explain this arrhythmic complication. Firstly, POAF may be associated to or be a surrogate marker of inflammatory stimuli involved in cardiac surgery [32, 33]. The CABG procedure involves manipulation of the heart and pericardium, which may place the thoracic cavity under surgical stress, inducing an inflammatory response and release of proinflammatory cytokines. The inflammation response may also be triggered directly via surgical incision of the atrium, leading to ischaemia or scar tissue which may act as a substrate for AF [34]. Recent evidence for the potential link between thromboembolism and POAF comes from El-Chami *et al.* [22], who demonstrated that POAF patients receiving warfarin experienced a 22% relative reduction in mortality compared with POAF patients without warfarin at discharge. Another proposed mechanism for POAF following CABG includes autonomic imbalance and sympathetic activation. Several studies have demonstrated a significant association between elderly cardiac surgery patients and increased circulating catecholamine levels [35]. This may translate into an increased sinus rate, atrial ectopic activity and heart rate variability, preceding the No-POAF [36, 37]. Some have proposed that based on this background, the prescription of beta-blockers may provide an antiarrhythmic effect and reduce POAF incidence following CABG [11, 38]. The present meta-analysis results do not support this, with no significant difference in beta-blocker use in POAF versus No-POAF groups. Oxidative stress may also play a role in the mechanisms of POAF following coronary bypass surgery. The CABG procedures involve a reperfusion stage, which induces oxidative stress in the patient that is directly related to the severity of the ischaemic period [39] and the left ventricular ejection fraction [40]. This may generate localized and systemic oxidative stress, thus inducing AF [41, 42]. While the causative mechanisms underlying POAF are still not clear, it is evident that this is a complex complication of multifactorial aetiology and is significantly associated with long-term mortality and morbidity. Future avenues of research should focus on the underlying pathophysiology of POAF, which may give rise to an effective way of reducing late mortality, rather than on more aggressive treatment options.

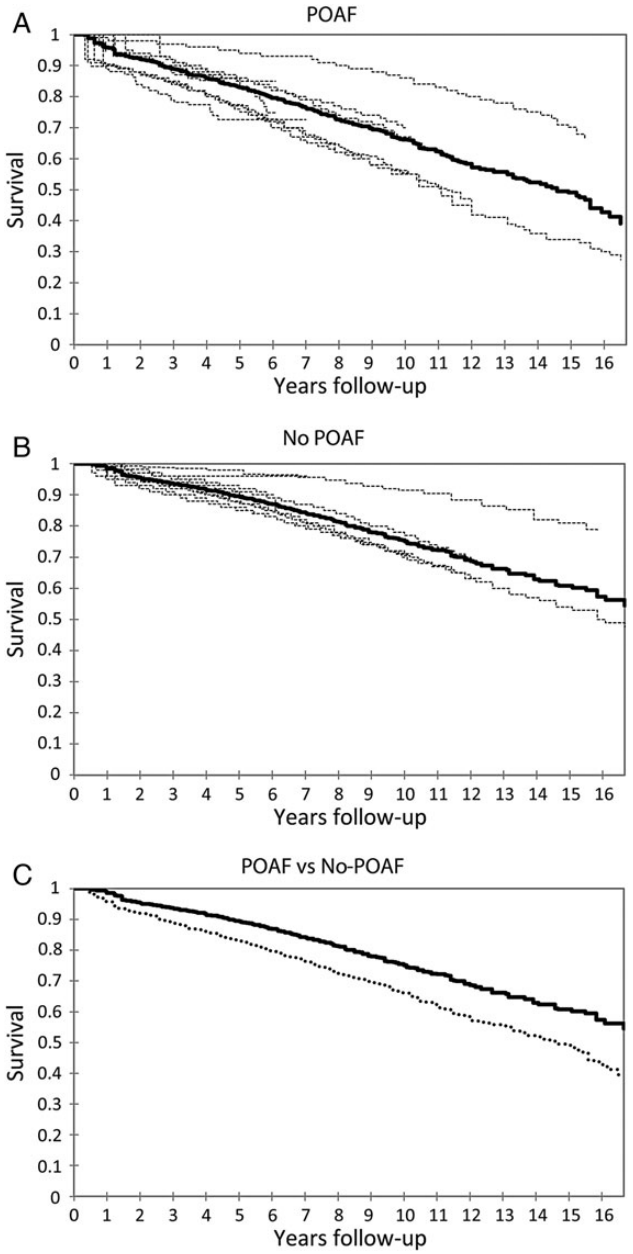

Figure 5: Overall Kaplan–Meier survival curves based on reconstructed individual patient data. (**A**) Long-term survival of the POAF cohort after coronary artery bypass grafting, reconstructed from 16 601 patients and presented. (**B**) Long-term survival of the No-POAF cohort after coronary artery bypass grafting, reconstructed from 52 917 patients. (**C**) Aggregated survival curve for No-POAF (solid) compared with POAF (dotted) (n = 69 518). Dashed lines represent Kaplan–Meier curves of individual studies, while the solid line represents the aggregate reconstructed survival data of the entire cohort. No-POAF: new-onset postoperative atrial fibrillation.

Strengths and limitations

The present meta-analysis is constrained by several limitations. First, this is a systematic review of predominantly retrospective, observational studies. Such study designs compare POAF and No-POAF cohorts that are unmatched, which may intrinsically be biased by other postoperative complications for which POAF is acting as a surrogate marker. Variations in population profiles between the study is another limiting factor, with some studies [22] only investigating long-standing persistent AF patients, while other studies investigated both paroxysmal and persistent forms. Rate and rhythm control, and anticoagulation protocols on follow-up was not consistently reported among the studies, and as such, it is difficult to definitively conclude whether increased long-term mortality in the POAF group is due to new-onset arrhythmia or poor management of underlying thromboembolic risk. Such variations may be responsible for significant heterogeneity observed in pooled complication rates. Second, the definition and inclusion/exclusion criteria for AF varied among the included studies, undermining the validity of reported incidence and follow-up POAF rates. For example, El-Chami *et al.* [22] defined new-onset AF according to the Society of Thoracic Surgery recommendations, which is the occurrence of POAF or atrial flutter requiring treatment in the form of beta-blockers, calcium-channel blockers, amiodarone, anticoagulation or cardioversion. In contrast, Ahlsson *et al.* [13] defined POAF as an ECG-verified episode lasting greater than 1 min during the first seven postoperative days. The former definition may also potentially exclude patients with short self-limiting fibrillation episodes, or those who did not receive medical or cardioversion treatment. Third, it is difficult to conclude whether No-POAF is an independent contributor to long-term mortality. Certainly, some risk factors identified in the present analysis including age, male gender, heart failure and peripheral vascular disease are also common to early mortality [11]. As such, delineating whether late mortality is due to the previous background of cardiovascular complications versus No-POAF is challenging and will require further investigation for validation. Finally, the inherent assumption of constant censoring when reconstructing individual patient survival data based on an iterative algorithm [14] may undermine the accuracy of the reported aggregate survival rates on follow-up.

The present study has several important strengths. Firstly, this updated meta-analysis is based on studies that report long-term aggregate survival rates for POAF versus No-POAF cohorts, instead of focusing on early and medium-term follow-up and overall effect-size reports. To provide the most up-to-date aggregated survival rate on follow-up, validated iterative statistical methods to solve inverted Kaplan–Meier solutions [14] and digitising software were used to determine as accurately as possible reconstructed individual patient data from each included study.

Furthermore, another limitation is the variability with which POAF was defined by different studies, and the diverse covariates for which POAF was adjusted for. When possible, pooled estimates of HR for overall survival were presented based on multivariate-adjusted HRs adjusted for multiple risk factors for AF. Sensitivity metaregression analysis did not show that the overall effect size was significantly influenced by any particular one study. There was also inconsistency between the studies in terms of adjustment for concomitant valvular surgery, and medications that may influence POAF such as amiodarone, calcium-channel blockers and statins. Ideally, the observational studies included in this meta-analysis should have similarly performed an adjusted analysis for relevant covariates for each studied outcome. Adjusted analysis was not feasible for pooled results from all included studies and this may lead to residual confounding in the observed observations.

Another constraint in this study is the non-standardized, inconsistent reporting of outcomes and complications. The extent to which POAF is associated with long-term AF is influenced by the rate of AF recurrence. This outcome was not addressed by the included studies in the long term, which limits the validity of our analysis.

Conclusions

New-onset AF following coronary bypass surgery is associated with significantly higher risk of mortality in short- and long-term follow-up. This difference in survival rate remains even up to the 15-year postoperative follow-up. Whether this association is causal or whether AF is only a marker for underlying cardiovascular disease remains to be elucidated in future studies. However, current evidence suggests the need for stricter surveillance and monitoring of POAF following coronary bypass surgery.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Conflict of interest: none declared.

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