Short- and long-term mortality associated with new-onset atrial fibrillation after coronary artery bypass grafting: A systematic review and meta-analysis

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Objectives: Our objectives were to evaluate short- and long-term mortality associated with new-onset atrial fibrillation after coronary artery bypass grafting and to identify preoperative and intraoperative patient characteristics associated with new-onset atrial fibrillation.

Methods: Three independent investigators comprehensively reviewed the literature using Medline from 1960, Web of Science from 1980, and Scopus from 1960. All searches were done through December 2009. Selected cohort studies were used to evaluate associations between new-onset atrial fibrillation after coronary artery bypass grafting or coronary bypass plus valve and short-term mortality (defined as 30-day or in-hospital mortality) and long-term mortality (defined as mortality $\geq$ 6 months). We excluded studies involving atrial flutter, off-pump coronary bypass, and isolated valve surgery. Heterogeneity among studies was accounted for by meta-analysis with random-effects models.

Results: Eleven studies (n = 40,112) met our inclusion criteria. New-onset atrial fibrillation was associated with higher short-term mortality (3.6% vs 1.9%; odds ratio [OR], 2.29; 95% confidence interval [CI], 1.74–3.01; $P < .00001$; heterogeneity of effects, $P = .002$). Mortality risks at 1 year and 4 years were 2.56 (95% CI, 2.14–3.08) and 2.19 (95% CI, 1.97–2.45; $P < .0001$), respectively. Older age, lower ejection fraction, history of hypertension, heart failure, prior stroke, peripheral arterial disease, and longer cardiopulmonary bypass and aortic clamp times were associated with new-onset atrial fibrillation. Preoperative use of ß-blockers reduced occurrence of new-onset atrial fibrillation (OR, 0.94 [95% CI, 0.88–1.01; $P = .08$]), whereas angiotensin-converting enzyme inhibitors increased it (OR, 1.20 [95% CI, 1.11–1.29], $P < .00001$).

Conclusions: New-onset atrial fibrillation after coronary artery bypass grafting appears to increase short- and long-term mortality. Preoperative use of ß-blockers, avoidance of angiotensin-converting enzyme inhibitors, and shorter cardiopulmonary bypass and aortic clamp times potentially reduce occurrence of new-onset atrial fibrillation. (J Thorac Cardiovasc Surg 2011;141:1305-12)

New-onset atrial fibrillation (AF) remains the most common complication after cardiac surgery, with little change over the past 2 decades. It occurs in 25% to 40% of patients after coronary artery bypass grafting (CABG) and in up to 62% after a combined CABG and valve procedure.[1]

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Disclosures: Authors have nothing to disclose with regard to commercial support.
R.K. and A.V.H. have contributed equally to this study.
Received for publication May 19, 2010; revisions received Sept 20, 2010; accepted for publication Oct 24, 2010; available ahead of print Jan 19, 2011.

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0022-5223/$36.00

doi:10.1016/j.jtcvs.2010.10.040

New-onset AF is widely known to increase morbidity after cardiac surgery,[2-5] and several studies have shown increased in-hospital and long-term mortality, but this association is not well established or clearly understood.[2-8] However, other studies have not reported new-onset AF to have an independent effect on in-hospital mortality.[9] Additionally, information related to new-onset AF comes mostly from single-institution studies. Therefore, the primary purpose of our meta-analysis was to evaluate the short- and long-term mortality of new-onset AF after CABG. Secondarily, we also evaluated preoperative, intraoperative, and postoperative variables associated with the occurrence of new-onset AF.

METHODS

Study Selection

We conducted a comprehensive literature search using Medline from 1960 through December 2009, The Web of Science from 1980 through December 2009, and Scopus from 1960 through December 2009. We

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Abbreviations and Acronyms

ACEI	= angiotensin-converting enzyme inhibitors
AF	= atrial fibrillation
CABG	= coronary artery bypass grafting
CI	= confidence interval
COPD	= chronic obstructive pulmonary disease
CPB	= cardiopulmonary bypass
DM	= diabetes mellitus
HF	= heart failure
IABP	= intra-aortic balloon pumping
LVEF	= left ventricular ejection fraction
MI	= myocardial infarction
OR	= odds ratio
PAD	= peripheral arterial disease

restricted our search to observational cohort studies and used the following key words: AF, cardiac surgery or cardiac surgical procedures or CABG surgery, mortality or death or outcomes, and determinants or risk factors. We also used MeSH and TIAB terms for the Medline search. All published studies that evaluated the occurrence of short-term (in-hospital or within 30 days) and long-term ($\geq$6 months) mortality in patients with new-onset AF after CABG with or without valve surgery were identified. In these studies, new-onset AF was defined as persistent AF of any duration at any time postoperatively by physician assessment on the basis of a rhythm strip or 12-lead electrocardiographic recording. Results of the combined search were limited to studies of adult humans published in English, Spanish, French, and German.

A list of retrieved articles was reviewed independently by 3 investigators (R.K., I.M., and A.V.H.) to choose potentially relevant articles. When multiple articles for a single study had been published, we used the latest publication and supplemented it, if necessary, with data from earlier publications. Only studies that clearly identified mortality and perioperative variables in tables or text for both new-onset AF and non–new-onset AF groups were included in the final data set. We excluded studies of atrial flutter and tachycardia, off-pump CABG procedures, and isolated valve surgery. All studies in which the main purpose of the publication was to evaluate a treatment or intervention were also excluded, unless preoperative or intraoperative information was useful for the purpose of our study.

Data Extraction

Data were extracted by 3 investigators (I.M., A.V.H., and R.K.) and the results compiled. Disagreement was resolved by consensus. Using a standardized data extraction form, we collected information on lead author, publication year, study design, sample size, and proportion of patients with early and late mortality. The following preoperative summary information was collected from each study for the new-onset and non–new-onset AF groups: age, gender, history of hypertension, myocardial infarction (MI), heart failure (HF), diabetes mellitus (DM), chronic renal insufficiency, stroke, peripheral arterial disease (PAD), chronic obstructive pulmonary disease (COPD), and smoking; left ventricular ejection fraction (LVEF), use of beta-blockers (ß-blockers), angiotensin-converting enzyme inhibitors (ACEI) and intra-aortic balloon pump (IABP). Information about intraoperative (cardiopulmonary bypass [CPB] time, use of IABP, aortic clamp time, and use of inotropes) and postoperative outcomes (length of hospital stay, respiratory failure, postoperative HF, stroke, and MI) was also collected.

Validity and Study Quality Assessment

Prospective cohort studies were considered to be of higher quality than retrospective cohort studies. Case–control studies that were specifically designed to assess the influence of risk factors on occurrence of new-onset AF were considered to be of higher quality than studies that used a nested case–control design, either by identifying cases of new-onset AF by hospital discharge registers or by using existing patient registries.

Statistical Analysis

First, we evaluated the association between new-onset AF after CABG and short- and long-term all-cause mortality. We used the Mantel–Haenszel method to calculate pooled odds ratios (OR) and 95% confidence interval (CI) methods for mortality.[10] Because mortality statistics are scarce and the proportion of new-onset AF patients low, the Mantel–Haenszel method was preferred. We also used DerSimonian and Laird random effects models, and statistical heterogeneity was evaluated as described elsewhere.[11] Publication bias was assessed graphically with funnel plots. We did not have access to individual patient-level data, and therefore no adjustment was possible for potential confounders of the association between new-onset AF and mortality. We used Review Manager (RevMan, version 5.0 for Windows, Oxford, United Kingdom; The Cochrane Collaboration, 2008).

Long-term mortality was reported at different time points (6 months, 1 and 4 years). We calculated unreported mortality from the reported Kaplan–Meier curves when available. With the exception of one, most studies did not report the number of patients at risk per time point, which discount patients who died or were lost to follow-up, and we could not use this information in the analysis. Given the circumstances under which IABP is used, we chose to combine the reported intraoperative and postoperative use for purposes of analysis. Preoperative IABP use was analyzed separately.

Sensitivity Analysis

To explore the strength of the association between new-onset AF and mortality, we removed studies with fewer than 500 patients with new-onset AF, removed studies whose populations underwent CABG plus valve surgery, and used fixed-effects models. After exclusion of studies with fewer than 500 patients, a total of 38,292 patients remained of whom 28,800 underwent CABG only. No differences were found between random and fixed models, and only random-effects models are reported.

We evaluated the association between patient characteristics (preoperative and intraoperative) and new-onset AF. We used the Mantel–Haenszel method to calculate pooled OR for categorical characteristics or mean difference for continuous characteristics and their 95% CIs. Also, because statistically significant clinical heterogeneity among studies was expected, we used the DerSimonian and Laird random-effects models. Statistical heterogeneity of effects was evaluated with the Cochran χ^2 test and the I^2 statistic. The overall effect was calculated with the Z test. Finally, we described the associations between postoperative outcomes and new-onset AF, which do not necessarily have a temporal relationship.

RESULTS

Study Characteristics

A total of 927 citations were identified and screened, of which 46 were retrieved for more detailed information (Figure 1). Of these, 34 did not fit our criteria, major reasons for exclusion being inclusion of patients with AF preoperatively, heart transplantation, valve-only procedures, and aortic surgery. We chose 12 studies. We did not get a response from the authors of 1 study, and it was eliminated from the analysis. Thus, we finally included 11 cohort studies[2-9,12-14] (n = 40,112; 5 prospective[2,5-8]), which were