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Clinical Risk Factors for Post-operative Atrial Fibrillation among Patients after Cardiac Surgery

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Abstract

Background—Post-operative atrial fibrillation (POAF) is a common arrhythmia following cardiac surgery and is associated with increased healthcare costs, complications, and mortality. The etiology of POAF is incompletely understood and its prediction remains suboptimal. Using data from published studies, we performed a systemic review and meta-analysis to identify preoperative clinical risk factors associated with patients at increased risk for POAF.

Methods—A systematic search of PubMed, MEDLINE, and EMBASE databases was performed.

Results—Twenty-four studies that reported univariate analysis results regarding POAF risk factors, published from 2001 to May 2017, were included in this meta-analysis with a total number of 36,834 subjects. Eighteen studies were carried out in the USA and Europe and 16 studies were prospective cohort studies. The standardized mean difference (SMD) between POAF and Non-POAF groups was significantly different [reported as (SMD: 95% CI)] for age (0.55: 0.47 to 0.63),

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Author contributions are as follows:

- 1) KY, NH, and DD devised the study design and conception. KY, NH, and DD analyzed and interpreted data.
- 2) KY, NH, and DD drafted the manuscript and CC, RR, NH, and DD revised it critically.
- 3) All authors approved the final version of the manuscript.

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Conflict of interest statement

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left atrial diameter (0.45: 0.15 to 0.75), and left ventricular ejection fraction (0.30: 0.14 to 0.47). The pooled odds ratios [(reported as (OR: 95% CI)) demonstrated that heart failure (1.56: 1.31 to 1.96), chronic obstructive pulmonary disease (1.36: 1.13 to 1.64), hypertension (1.29: 1.12 to 1.48), and myocardial infarction (1.18: 1.05 to 1.34) were significant predictors of POAF incidence, while diabetes was marginally significant (1.06: 1.00 to 1.13).

Conclusion—The present analysis suggested that older age and history of heart failure were significant risk factors for POAF consistently whether the included studies were prospective or retrospective data sets.

Keywords

Atrial Fibrillation; Cardiac Surgery; Odd Ratio; Standardized Mean Difference

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia following cardiac surgery and post-operative atrial fibrillation (POAF) is associated with prolonged hospitalization, increased healthcare costs, complications, and long-term mortality [1–25]. Kosmidou et al.[26] reported POAF after coronary artery bypass surgery (CABG) was associated with a 4-fold increase of 3-year stroke risk and 3-fold increase of all-cause mortality. Therefore, understanding the causes of POAF and reducing the risk of POAF will lead to improved care of cardiac surgery patients. On the other hand, the etiology of POAF is incompletely understood and its prediction remains suboptimal. Several risk factors [27,28], biomarkers [29,30], and genetic variants [31,32] have been investigated and linked to POAF but have not proven to be particularly sensitive in predicting which patients will develop POAF. Risk indexes that attempt to predict an individual's risk for developing POAF have been developed [29,33–36], but these too suffer from a lack of specificity predicting which patients will develop POAF.

Electrical cardioversion or pharmacological interventions to restore sinus rhythm have been reported to yield improvements in symptoms and quality of life [37,38]. However, these interventions demonstrated the possibility of the inherent adverse side effects related to the interventions outweighing the benefits of AF suppression on postoperative outcomes [39]. Identifying specific patients at high risk for developing POAF may help to define a population that is more likely to benefit from anti-arrhythmic drugs or other preventive strategies. While there are many studies that individually evaluate the clinical risk factors for POAF, there is disagreement as to which clinical factors are associated with the greatest risk for POAF. Therefore, we conducted a systematic review and meta-analysis to identify the preoperative risk factors that are associated with POAF occurrence.

2. Methods

2.1. Search Strategy

A systematic electronic search was performed on the PubMed, MEDLINE, and EMBASE databases. We combined the terms: “atrial fibrillation”, “post-operative atrial fibrillation”, “cardiac surgical procedure”, and “cardiac surgery” as either keywords or MeSH terms (See

Fig 1). The search included the time period between 2001 and May 2017 was conducted without language restrictions. To achieve maximum sensitivity of the search strategy and identify all studies, the reference lists of all retrieved articles were manually screened for further identification of potentially relevant studies. All identified articles were systematically assessed using the inclusion and exclusion criteria.

2.2. Selection criteria

The major inclusion criteria were: (i) patients in the study underwent cardiac surgery; (ii) non-interventional study; (iii) the main outcomes included the incidence of new onset of AF; (iv) data available regarding clinical patient characteristics; (v) the data included information about patients with POAF and without POAF. The major reasons for exclusion of studies were: (i) patients with prior History of AF (ii) overlapping data sets; (iii) patients aged <18years old; (iv) data published in the form of abstracts without peer-reviewed publication of manuscripts.

2.3. Data extraction

All data were extracted from article texts, tables and figures. Two investigators independently reviewed each retrieved article (D.D. and K.Y.). Discrepancies between the two reviewers were resolved by discussion and consensus with a third reviewer (N.H.). These points include: (i) clear identification of study population, (ii) clear definition of outcome and outcome assessment, (iii) independent assessment of outcome parameters, (iv) selective loss during follow-up, and (v) important confounders or prognostic factors or both identified.

2.4. Statistical analysis

The odds ratios (ORs), standard errors (SEs), and the 95% confidence intervals (CIs) from the univariable logistic regression model in each study were collected during the data extraction phase. Pooled ORs for each risk factor were calculated using the inversed variance (IV) random effect (RE) method [40]. The standardized mean difference (SMD) was used to compare the continuous variables (demographic features and clinical risk variables) between patients with and without POAF. To calculate the SMD, Hedges' adjusted g formula was used, which includes an adjustment for small sample bias. The calculation of the SMD is given by:

$$SMD_i = \frac{m_{1i} - m_{2i}}{s_i} \left(1 - \frac{3}{4N_i - 9} \right),$$

where m_{1i} is the mean for those with POAF, m_{2i} is the mean for those without POAF, s_i is the pooled standard deviation (SD), and $N_i = n_{1i} + n_{2i}$ is the total number of observations where n_{1i} and n_{2i} are the total number of subjects with and without POAF, respectively [41]. The SE of SMD is calculated as:

$$SE(SMD_i) = \sqrt{\frac{N_i}{n_{1i}n_{2i}} + \frac{SMD_i^2}{2(N_i - 3.94)}}.$$

All statistical tests were two-sided, and results with p-value lower than 0.05 were considered as statistically significant. Data analyses were carried out using Review Manager (Copenhagen, Denmark) [41], or RevMan, version 5.3, SAS (SAS Institute Inc., Cary, NC, USA) version 9.4 and Stata (Stata Corp., College Station, TX, USA) version 14.

2.5. Assessment of heterogeneity

To check for heterogeneity, for each analysis we first calculated the pooled OR and SMD estimate using a random effects model. The I^2 statistic tests the null hypothesis that each study is evaluating the same effect. Large I^2 values indicate high heterogeneities.

2.6. Assessment of publication bias

Each of the pooled analysis outcomes was quantitatively assessed for publication bias using the Egger's test.

3. Results

Twenty-four studies reporting POAF incidence were included in this meta-analysis with a total of 36,834 subjects (Table 1). Sixteen out of the 24 studies (66.7%) used prospective study design. Most studies (18 out of 24, or 75.0%) were conducted in the United States or Europe. The number of patients ranges from 57 (Dogan et al. [11]) to 18,517 (El-Chami et al. [12]). Incidence of POAF in included studies was 28.0% (95% CI: 23.5 to 32.6). Males dominated in most studies (20 out of 24, or 83.3%). On pump CABG were involved in 14 studies, while off pump CABG were used in 10 studies.

Table 2 summarizes the results of our meta-analysis. Among the four continuous variables being examined, age, left atrial diameter (LAd), and left ventricular ejection fraction (EF) were found to be statistically significantly different between patients with and without POAF.

Age data was analyzed from sixteen studies and 21,665 patients. The SMD was calculated to be 0.55 (95% CI: 0.47 to 0.63), with POAF patients having a greater mean in age of 5.45 (95% CI: 4.29 to 6.61) years compared to patients that did not have POAF. There was a moderate heterogeneity ($I^2 = 25\%$) in this analysis. See Fig. 2A.

LAd data was analyzed from eight studies and 949 patients. The estimated SMD was 0.45 (95% CI: 0.15 to 0.75), with POAF patients having a larger mean in LAd of 2.01 (95% CI: 1.03 to 2.99) mm compared to patients without POAF. There was a large heterogeneity ($I^2 = 71\%$) in this analysis (Fig. 2B).

EF data was analyzed in eleven studies and 19,961 patients. The estimated SMD was 0.30 (95% CI: 0.14 to 0.47), with POAF patients having a lower mean in EF by 3.01% (95% CI:

1.43 to 4.58) lower than patients that did not have POAF. There was a moderate heterogeneity ($I^2 = 57\%$) in this analysis. See Fig. 2C.

Among the dichotomous clinical factors, History of heart failure (HF), chronic obstructive pulmonary disease (COPD), hypertension, History of myocardial infarction (MI) and diabetes were found to be the significant risk factors for POAF.

History of HF was analyzed in seven studies and 32,841 patients with a total number of 6,729 POAF events. The pooled ORs was 1.56 and (95% CI: 1.31 to 1.86), in favor of the subjects without a History of HF. Patients with a HF history are expected to have a 56% higher odds of POAF than those without HF. There was a relatively large heterogeneity ($I^2 = 62\%$) in this analysis. See Fig. 3A.

Prevalence of COPD was evaluated from thirteen studies and 34,302 patients with a total number of 7,067 POAF events. The pooled OR was 1.36 and (95% CI: 1.13 to 1.64), in favor of the subjects without COPD. On average, patients with COPD have a 36% higher odds of POAF than those without COPD. There was a moderate heterogeneity ($I^2 = 40\%$) in this analysis. See Fig. 3B.

Hypertension data was analyzed from nineteen studies and 35,498 with a total number of 7,356 POAF events. The pooled OR was 1.29 and (95% CI: 1.12 to 1.49), in favor of the subjects without POAF. On average, patients with hypertension are expected to have a 29% higher odds of POAF when compared with their counterparts without hypertension. There was moderate heterogeneity ($I^2 = 39\%$) in this analysis. See Fig. 3C.

History of MI was analyzed in ten studies and 33,177 patients, with a total number of 6,815 POAF events. The pooled OR was 1.18 and (95% CI: 1.05 to 1.34), in favor of the subjects without the History of MI. Patients with the History of MI are expected to have an 18% higher odds of POAF than those without History of MI. There was a moderate heterogeneity ($I^2 = 39\%$) in this analysis. See Fig. 3D.

Twenty-one studies and 36,059 patients were included in the analysis of diabetes, with a total number of 7494 POAF events. There is a marginally significant association between diabetes and POAF, with a pooled ORs of 1.06 and (95% CI: 1.00 to 1.13), in favor of the subjects without the diabetes. Patients with diabetes are expected to have a 6% higher odds of POAF than those without diabetes. There was a very small heterogeneity ($I^2 = 3\%$) in this analysis. See Fig. 4.

Body mass index (BMI) data, β -blocker use, patient gender, and dyslipidemia were also analyzed with respect to POAF incidence. These factors did not reach statistical significance in our meta-analysis. See Fig. 5A, 5B, 5C, and 5D.

Because of the types of included studies, we divided all studies into prospective and retrospective design groups (Table 3). In this sub-analysis, Age and History of HF were consistently significant predictors for POAF incidence despite of study design. On the other hand, LAd and EF were not significant predictors in retrospective design group. Moreover,

in prospective design group, COPD, HT, and History of MI also did not predict the incidence of POAF significantly.

In order to evaluate the sensitivity of our analysis to surgery type, we also conducted a sub-group analysis by analyzing the CABG studies and valve surgery studies separately (Table 4). The sub-analysis of CABG showed that large LA diameter was not a significant predictors of POAF but that the other clinical risk factors were similar to original analysis. The sub-group analysis of the valve surgery studies showed that older age and β blocker use were significant predictors of POAF. The difference in the sub-group analysis are likely due to the smaller sample size of the groups, particularly in the valve surgery studies.

4. Discussion

The primary findings of this study are as follows: 1) Older age (as a continuous measurement), increased LAd, and lower EF were associated with increased POAF incidence. 2) Binary risk factors of a History of HF, COPD, hypertension, MI, and diabetes were associated with increased POAF incidence. 3) Findings about age and History of HF were consistent whether the included studies were prospective or retrospective data sets.

The value of this meta-analysis is that while individual studies may not show a significant relationship between clinical variables and POAF incidence, pooling results from many studies can show relationships that are not consistent in individual studies. Some of the clinical factors in this analysis were predictably significant. For example, 12 of the 16 studies analyzed for age demonstrated that POAF patients were significantly older than those without POAF, and the other 4 studies trended towards older age in POAF patients. However, LA diameter was significantly larger in only 2 of 8 studies, with 1 of the 8 studies showing a lower average LA diameter. The meta-analysis found larger LA diameter to be significantly associated with POAF incidence.

Advanced age is considered an independent predictor for POAF after cardiac surgery as well as AF incidence outside of the cardiac surgery population [42]. Patients with advanced age experience remodeling in the atrial tissue including changes in ion channel function and distribution [43], systemic inflammation [3,6,9,21], impulse propagation [7,8,10,13], fibrosis distribution [15,16], and structural substrate [4,17,19,24], which lead to increased POAF inducibility and burden with increased age. Since age related remodeling is chronic and slow, older patients undergoing cardiac surgery likely have developed the substrate for increased POAF inducibility and burden. With the increased inflammation and sympathetic tone experienced by cardiac surgery patients, underlying age related structural remodeling may facilitate the new onset of POAF.

LAd may be increased due to patient characteristics such as age, gender, or body size. Pathophysiological conditions such as mitral valve regurgitation, arteriovenous fistula, and left to right shunt that lead to pressure and/or volume overload may also lead to increased LAd. Increased LAd has been associated with increased AF incidence in the general population [42], and in this meta-analysis, we have found that patients with POAF had larger

LAd than the patients without POAF. Increased atrial dimension may lead to increased AF burden.

COPD is associated with an increased incidence of new onset of POAF as well as non-surgical AF. According to Mangnas et al. [44], patients with severe COPD experienced POAF more frequently than patients with mild to moderate COPD. However, Fuster et al. [45] also reported severity of COPD was correlated with pulmonary infections and length of hospital stay while the incidence of POAF after CABG was not significantly associated with significant COPD. The specific mechanisms by which POAF and COPD are associated are currently not known.

Hypertension is a leading cause of cardiovascular disease and is the most prevalent comorbidity in patients with AF [46]. Hypertension may induce atrial cardiomyopathy, increased LAd, and atrial stretch, which induce structural and electrophysiological changes conducive to AF onset and burden. Gap junction remodeling associated with hypertension may lead to conduction abnormalities and ectopic firing, contributing to both the substrate and triggers required for AF onset and maintenance [47].

Patients with a History of MI are at increased risk for non-surgical AF [37,42]. Patients with coronary artery disease and History of MI may be at risk for compromised atrial perfusion, which has been proposed as a mechanism for atrial fibrosis deposition and electrophysiological remodeling [48]. Coronary artery disease may also lead to heterogeneous atrial blood flow and variations in dispersion of refractoriness. Since many of the cardiac surgery patients have a History of MI, this risk factor is of particular importance to POAF incidence. Particularly CABG patients may have the substrate and heterogeneous arterial blood flow that places them at higher risk for POAF.

Patients with diabetes are 50% more likely to have nonsurgical AF [42]. Diabetes is associated with increased atrial fibrosis, which has been shown to increase AF burden [49]. Autonomic dysfunction, particularly with an imbalance towards increased sympathetic tone, is prevalent in diabetic patients and may play a key role in the triggering or initiating AF [50]. In our meta-analysis, diabetes was only marginally significantly associated with POAF incidence, and patients with diabetes only have a 6% increase in risk of POAF incidence as compared to patients without POAF.

Other factors, including β -blocker use, gender, and dyslipidemia were not significantly different in patients with POAF from those that did not experience POAF. While BMI has been shown to be a clinical risk factor for non-surgical AF [51,52], our meta-analysis did not show increased BMI to be associated with increased POAF incidence. Another study determined that increased BMI led to increased AF risk, but when BMI was adjusted for LAd, BMI was no longer associated with AF risk [53]. BMI may be a secondary marker for atrial dilatation and stretch, but alone it may not be a direct measure of substrate remodeling in the atria that would lead to increased POAF for surgical patients.

Preoperative β -blocker use has been recommended before CABG as first-line therapy in guidelines because preoperative β -blocker use has been shown to reduce the incidence of POAF [54]. However, in this meta-analysis and subanalysis, β -blocker was not associated

with POAF incidence. One reason was that this meta-analysis was not about assessing the effect of preoperative β -blocker use in prospective randomized controlled trial. β -blockers may be administered more often in patients with higher age, lower EF, and hypertension, negating the benefits of β -blocker administration. Another reason was that the dose and type of β -blocker were not consistent in this analysis. DoNicolantonie et al. [55] concluded that, compared with metoprolol, carvedilol significantly reduced the incidence of POAF in patients undergoing CABG.

5. Study Limitations

Our study contains several limitations. First, the type of studies in this meta-analysis is a mixture of prospective and retrospective studies. The unadjusted odds ratios from the univariable analysis in retrospective studies were more likely to be biased due to confounding. To correct for this possible confounding, we performed a sensitivity analysis that includes only the prospective studies in all analyses. The results of all these analyses were similar to those incorporating all studies.

Second, studies in our meta-analysis include different type of surgeries. Among these studies, the most common surgery type is valve surgery and CABG. In addition, studies we considered in the meta-analysis often included a mixture of several surgery types. Types of surgeries being used in each study can be found in Table 1. Our sensitivity analysis showed that the meta-analysis results was sensitive to the surgery type. Hence, caution should be used to generalize our study finding to one specific surgery type.

Third, our meta-analysis used studies from different geographic populations that can be quite different in genotypes. There is also a large variability in terms of sample sizes. Two studies had large sample sizes of more than 13,000 patients, while four studies had a sample size less than 100.

Fourth, the criteria for defining the POAF and monitoring methods varied across studies. Some studies defined POAF as any incidence of AF during the follow-up period while others defined it as AF lasting more than 1 hour. Also, patients in most included studies were continuously monitored until discharge but in some studies, heart rhythm was continuously recorded for the first 48 to 72 hours and monitored every 4 hours. Moreover, follow-up time varied substantially, with some studies following patients only during their ICU stay following surgery, with others utilized monitoring for up to 1 month following cardiac surgery.

Fifth, some meta-analyses of pooled OR and SMD has a relatively large I^2 value ($> 60\%$). For example, the SMD of LAd and EF as well as the pooled OR of History of HF. These indicate a relatively large heterogeneity in the studies used in these meta-analyses. Caution should be used when trying to generalize these results.

6. Conclusion

Advanced age, increased LA diameter, reduced LVEF, and a History of HF, COPD, hypertension, and a History of MI are all associated with increased risk of POAF. Patient

characteristics including advanced age and a History of HF were at increased risk for developing POAF following cardiac surgery, whether the data come from prospective or retrospective studies. Body mass index, β -block use, gender, and dyslipidemia were not associated with POAF incidence.

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Figure 1:
Flowchart of the literature search strategy.

Figure 2:

Forest plots showing std. mean difference of age in years (A), LAd in mm (B), and left ventricular EF (C) in percentage between patients with POAF without POAF.

POAF=post-operative atrial fibrillation, SD=standard deviation, IV=inverse variance, CI=confidence interval, M-H=Mantel-Haenszel, LAd=left atrial diameter, EF=ejection fraction, HF=heart failure, BMI=body mass index, COPD=chronic obstructive pulmonary disease, MI=myocardial infarction,

Figure 3.

Forest plot showing the pooled POAF odds ratios for HF (A), COPD (B), hypertension (C), and MI (D).

Abbreviations as in Figure 2

*Large OR because of the small N for patients with COPD

Figure 4:
 Forest plot showing the pooled odds ratio for diabetes.
 Abbreviations as in Figure 2

Figure 5:

Forest plot showing std. mean difference of BMI (A) in kg/m^2 and the pooled odds ratio for β -blocker use (B), gender (C), and dyslipidemia (D).

Abbreviations as in Figure 2

Characteristics of Included Studies

Table 1:

Author (year)	Country	Type of Study	Number of Subjects	Number of POAF	Incidence (%) of POAF (95% CI)	Number (%) of Male	Type of Surgery
Abdel-Massih (2012)	Lebanon	Prospective	113	18	15.9 (15.8, 16.0)	94 (83.2)	On pump CABG
Anderson (2017)	US	Prospective	324	77	23.8 (23.7, 23.9)	233 (71.9)	CABG or valve surgery
Antoniades (2009)	UK	Prospective	144	43	29.9 (29.8, 30.0)	120 (83.3)	Off pump CABG
Ba aran (2016)	Turkey	Prospective	90	23	25.6 (25.4, 25.8)	71 (78.9)	On or Off pump CABG
Bolesta (2015)	US	Retrospective	244	74	30.3 (30.2, 30.4)	103 (42.2)	Valve surgery
Bouchot(2015)	France	Prospective	100	34	34.0 (33.8, 34.2)	92 (92.0)	On or Off pump CABG
Budeus (2006)	Germany	Prospective	101	37	36.6 (36.4, 36.8)	79 (78.2)	On pump CABG
Çetin (2012)	Turkey	Prospective	272	62	22.8 (22.7, 22.9)	224 (82.4)	On or Off pump CABG
Choi (2009)	Korea	Prospective	315	66	21.0 (20.9, 21.1)	225 (71.4)	Off pump CABG
Di Gioia (2017)	Italy	Retrospective	134	41	30.6 (30.4, 30.8)	98 (73.1)	Valve surgery
Dogan (2007)	Turkey	Prospective	57	10	17.5 (17.3, 17.7)	37 (64.9)	On pump CABG
EL-Chami (2012)	US	Retrospective	18,517	3,486	18.8 (18.8, 18.8)	13,276 (71.7)	On or Off pump CABG
Gang (2004)	UK	Prospective	151	40	26.5 (26.4, 26.6)	126 (83.4)	On or Off pump CABG
Gode (2016)	Turkey	Prospective	90	15	16.7 (16.5, 16.9)	70 (77.8)	On pump CABG
Guo (2017)	China	Prospective	109	19	17.4 (17.3, 17.5)	38 (34.9)	CABG and myectomy
Hernández-Romero (2017)	Spain	Prospective	100	29	29.0 (28.8, 29.2)	77 (77.0)	CABG or valve surgery
Ngai (2016)	US	Retrospective	562	215	38.3 (38.3, 38.3)	229 (40.7)	On pump CABG and/or Valve
O'Neal (2013)	US	Retrospective	13,165	2,907	22.1 (22.1, 22.1)	9,281 (70.5)	On or Off pump CABG
Osranek (2006)	US	Prospective	203	84	41.4 (41.3, 41.5)	133 (65.5)	CABG and/or valve surgery
Park (2014)	Korea	Prospective	113	39	34.5 (34.3, 34.7)	81 (71.7)	On or Off pump CABG
Saskin (2017)	Turkey	Retrospective	662	153	23.1 (23.1, 23.1)	541 (81.7)	On or Off pump CABG
Shariff (2010)	US	Retrospective	757	144	19.0 (19.0, 19.0)	558 (73.7)	On pump CABG
Silva (2010)	Brazil	Prospective	448	145	32.4 (32.4, 32.4)	287 (64.1)	CABG or valve surgery
Takahashi (2014)	Japan	Retrospective	63	41	65.1 (64.7, 65.5)	23 (36.5)	Valve surgery
Total			36,834	7,802	28.0 (23.5, 32.6)	26,096 (70.8)	

POAF=post-operative atrial fibrillation, CABG=coronary artery bypass graft, CI=confidence interval

Table 2:

Summary of Meta-analysis Results

(a) SMDs				
Variables	I²	Number of studies	Number of subjects	Std. Mean Difference [IV, Random, 95% CI]
Age [3,4,6–15,17,19,22,24]	25%	16	21,665	0.55 [0.47, 0.63] *
LA diameter [1,3,7,8,11,14,15,24]	71%	8	949	0.45 [0.15, 0.75] *
Ejection Fraction [6–12,14,15,19,24]	69%	11	19,961	–0.30 [–0.47, –0.14] *
BMI [7,8,10–12,15,24]	0%	7	19,253	0.01 [–0.03, 0.04]
(b) Pooled ORs				
Variables	I²	Number of studies	Number of subjects	Odds Ratio [M-H, Random, 95% CI]
History of HF [5,12,13,18–20,23]	62%	7	32,841	1.56 [1.31, 1.86] *
COPD [2,5–9,12–14,18,19,22,24]	40%	13	34,302	1.36 [1.13, 1.64] *
Hypertension [2–15,18,19,21,22,24]	39%	19	35,498	1.29 [1.12, 1.48] *
History of MI [2,5–7,9,11–13,18,19]	39%	10	33,177	1.18 [1.05, 1.34] *
Diabetes [2–15,18–24]	3%	21	36,059	1.06 [1.00, 1.13] **
β-blocker use [2–10,13–15,18–22,24]	38%	18	17,037	1.13 [0.95, 1.36]
Male gender [2–15,17–22,24]	32%	21	36,173	0.98 [0.87, 1.11]
Dyslipidemia [3,6,8,10,13,15,19,21,23,24]	49%	10	2,286	1.03 [0.75, 1.41]

* significant difference at the 0.05 test level

** marginally significant difference at the 0.05 test level

IV=inverse variance, M-H=Mantel-Haenszel, BMI=body mass index, LA=left atrial, COPD=chronic obstructive pulmonary disease, MI=myocardial infarction, HF=heart failure, SMDs=standardized mean differences, ORs=odds ratios

Table 3:

Comparison between analysis in prospective and retrospective studies

(a) SMDs								
Prospective Study					Retrospective Study			
	I ²	Number of studies	Number of subjects	Std. Mean Difference [IV, Random, 95% CI]	I ²	Number of studies	Number of subjects	Std. Mean Difference [IV, Random, 95% CI]
Age	27	11	1,632	0.47 [0.34, 0.61]*	0	5	20,033	0.58 [0.55, 0.62]*
LA diameter	75	7	886	0.46 [0.12, 0.80]*	0	1	63	0.43 [−0.09, 0.96]
Ejection Fraction	38	8	1,247	−0.37 [−0.54, −0.19]*	25	3	18,714	−0.11 [−0.26, 0.05]
BMI	0	4	539	0.17 [−0.03, 0.37]	0	3	18,714	0.00 [−0.03, 0.04]
(b) Pooled ORs								
Prospective Study					Retrospective Study			
	I ²	Number of studies	Number of subjects	Odds Ratio [M-H, Random, 95% CI]	I ²	Number of studies	Number of subjects	Odds Ratio [M-H, Random, 95% CI]
History of HF	0	4	915	2.09 [1.53, 2.86]*	78	3	31,926	1.42 [1.18, 1.72]*
COPD	30	8	1,556	1.51 [0.91, 2.48]	56	5	32,746	1.31 [1.09, 1.58]*
Hypertension	20	12	1,956	1.21 [0.93, 1.58]	60	7	33,542	1.33 [1.13, 1.56]*
History of MI	53	7	1,251	1.41 [0.93, 2.15]	0	3	31,926	1.16 [1.10, 1.22]*
Diabetes	0	14	2,517	1.10 [0.90, 1.35]	24	7	33,542	1.07 [0.98, 1.17]
β-blocker use	27	12	2,012	0.95 [0.72, 1.26]	12	6	15,025	1.31 [1.14, 1.51]
Male gender	17	13	2,069	0.85 [0.65, 1.10]	33	8	34,104	1.06 [0.95, 1.18]
Dyslipidemia	45	7	1,427	1.03 [0.70, 1.51]	70	3	859	1.02 [0.48, 2.15]

* significant difference at the 0.05 test level

IV=inverse variance, M-H=Mantel-Haenszel, BMI=body mass index, LA=left atrial, COPD=chronic obstructive pulmonary disease, MI=myocardial infarction, HF=heart failure

Table 4:

Comparison between analysis in CABG and Valve Surgery

(a) SMDs		CABG				Valve Surgery			
	I ²	Number of studies	Number of subjects	Std. Mean Difference [IV, Random, 95% CI]	I ²	Number of studies	Number of subjects	Std. Mean Difference [IV, Random, 95% CI]	
Age	33	11	20,594	0.49 [0.39, 0.59]*	0	2	197	0.73 [0.42, 1.04]*	
LA diameter	92	6	777	0.39 [-0.25, 1.02]	0	1	63	0.43 [-0.09, 0.96]	
Ejection Fraction	79	7	19,452	-0.35 [-0.60, -0.11]*	0	2	197	-0.28 [-0.58, 0.02]	
BMI	0	4	18,947	0.00 [-0.03, 0.04]	0	2	197	0.12 [-0.18, 0.42]	
(b) Pooled ORs									
	I ²	Number of studies	Number of subjects	Odds Ratio [M-H, Random, 95% CI]	I ²	Number of studies	Number of subjects	Odds Ratio [M-H, Random, 95% CI]	
History of HF	45	4	31,946	1.57 [1.38, 1.79]*	0	1	244	0.68 [0.39, 1.19]	
COPD	50	9	33,468	1.29 [1.05, 1.59]*	36	2	307	1.44 [0.46, 4.52]	
Hypertension	44	13	34,421	1.31 [1.13, 1.52]*	53	3	441	1.54 [0.74, 3.18]	
History of MI	45	7	32,406	1.21 [1.07, 1.37]*	0	1	244	1.33 [0.38, 4.69]	
Diabetes	0	14	34,534	1.06 [1.00, 1.12]*	61	3	441	1.72 [0.65, 4.54]	
β-blocker use	50	12	15,960	1.01 [0.79, 1.29]	0	3	441	1.88 [1.22, 2.89]*	
Male gender	43	14	34,534	1.00 [0.86, 1.15]	29	3	441	0.82 [0.49, 1.39]	
Dyslipidemia	0	5	1,329	0.96 [0.73, 1.25]	82	2	197	1.03 [0.21, 5.09]	

* significant difference at the 0.05 test level

IV=inverse variance, M-H=Mantel-Haenszel, BMI=body mass index, LA=left atrial, COPD=chronic obstructive pulmonary disease, MI=myocardial infarction, HF=heart failure