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Postoperative outcomes of patients with chronic obstructive pulmonary disease undergoing coronary artery bypass grafting surgery

A meta-analysis

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a frequent comorbid disease in patients undergoing coronary artery bypass grafting (CABG) surgery, with an incidence ranging from 4% to 20.5%. Conventionally, COPD was recognized as a surgical contraindication to CABG. Because of the recent improvements in surgical techniques, anesthesia, and postoperative management, CABG has been performed more commonly in patients with COPD. However, studies have shown the various effects of COPD on postoperative morbidity and mortality after CABG, and this remains to be well defined.

Objectives: To compare the postoperative outcomes after CABG between patients with and those without COPD.

Methods: A systematic search was conducted in the Cochrane Library, PubMed, EmBase, and Ovid databases (until May 10, 2018). Studies comparing perioperative results and mortality outcomes after CABG between patients with and those without COPD were evaluated independently by 2 reviewers to identify the potentially eligible studies. Review Manager and STATA software were used for statistical analyses.

Results: No significant difference in the mortality rates were found between patients with and those without COPD. COPD was associated with a higher respiratory failure rate (odds ratio [OR] = 4.01; 95% CI: 1.19–13.51, $P = .03$; $P < .001$ for heterogeneity), higher pneumonia rate (OR = 2.92; 95% CI: 2.37–3.60, $P < .00001$; $P = .73$ for heterogeneity), higher stroke rate (OR = 2.91; 95% CI: 1.37–6.18, $P = .005$; $P = .60$ for heterogeneity), higher renal failure rate (OR = 1.60; 95% CI: 1.30–1.97, $P < .00001$; $P = .19$ for heterogeneity), and higher wound infection rate (OR = 2.16; 95% CI: 1.21–3.88, $P = .01$; $P = .53$ for heterogeneity) after CABG.

Conclusions: Patients with COPD were at higher risks for developing postoperative morbidities, particularly pneumonia, respiratory failure, stroke, renal failure, and wound infection. Although COPD was not associated with a higher risk of mortality, caution should be taken when a patient with COPD is indicated for CABG, considering the higher odds of postoperative complications involving the respiratory system and others.

Abbreviations: CABG = coronary artery bypass grafting, CIs = confidence intervals, COPD = chronic obstructive pulmonary disease, FEV1 = the forced expiratory volume in 1 second, FVC = forced vital capacity, ICU = intensive care unit, MD = mean difference, NOS = Newcastle–Ottawa scale, OR = odds ratios, RCT = randomized clinical trial.

Keywords: COPD, coronary artery bypass grafting, meta-analysis

1. Introduction

Chronic obstructive pulmonary disease (COPD) is the third leading cause of age-standardized death worldwide, with approximately 3.2 million patients dying from the disease.[1] COPD is an inflammatory disease of the airways, the alveoli, and the microvasculature, presenting with a persistent airflow limitation and a remodeling of small airways.[2] The featured lung tissue remodeling involves pulmonary and systemic inflammation, changes in mucosal tissue, fiber types and/or fibrosis, lung vascular remodeling, and angiogenesis. These pathological changes, especially the systemic inflammation and deregulated angiogenesis contribute to adverse effects on various extrapulmonary organs in COPD patients.[3,4] In the clinical work, COPD is a frequent comorbid disease in patients undergoing coronary artery bypass grafting (CABG), with the incidence ranging from 4% to 20.5%.[5,6] Conventionally, COPD was recognized as a surgical contraindication to CABG. In patients indicated for CABG, COPD was reported to be associated with increased postoperative mortality and morbidity, such as prolonged mechanical ventilation, respiratory failure, and atrial fibrillation.[7,8]

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Currently, because of the recent improvements in surgical techniques, anesthesia, and postoperative management, CABG has been performed more commonly in patients with COPD. Studies showed different effects of COPD on postoperative morbidity and mortality. Mortality rates were reported to be comparable between patients with mild to moderate COPD and those without COPD, whereas only severe COPD was associated with increased mortality risk.[9] Moreover, some studies have found that the mortality rate of patients undergoing CABG was not influenced by the severity of airflow obstruction, and COPD was not an independent risk factor for higher mortality and morbidity rates.[10,11] Thus, the present study was conducted to evaluate the perioperative results and mortality outcomes after CABG between patients with and those without COPD.

2. Methods

2.1. Inclusion and exclusion criteria

Studies were included on the basis of the following inclusion criteria:

1) The studies compared patients with and those without COPD undergoing CABG. COPD was confirmed by spirometry when the forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) was lower than 70% [based on the global initiative for chronic obstructive lung disease (GOLD) category] or from diagnosis or treatment records.[12]
2) At least parts data of the outcomes of interest regarding postoperative results and cardiopulmonary complications should be provided.
3) When populations across studies overlap, the study with better-quality would be included.
4) The studies were in English language (to secure the quality of included study).

The exclusion criteria for the studies were as follows:

1) Studies including patients undergoing simultaneous valve surgery with CABG or significant surgical procedure other than median sternotomy;
2) non-comparative studies;
3) studies with less than 10 patients in either group; and
4) unpublished studies, letters, conferences, reviews, and studies with unavailable full text or baseline data.

2.2. Search strategy for studies

A systematic search was conducted to identify studies investigating the effect of COPD on the perioperative results and survival outcomes of patients undergoing CABG. PubMed, EmBase, and Cochrane Library were searched until March 1, 2018. The following search terms and their combinations were adopted: (((Chronic obstructive pulmonary disease) or (Chronic obstructive lung disease)) or COPD), (((coronary artery bypass grafting) or (coronary artery bypass graft)) or (coronary artery bypass surgery)). During the process of study searching, the "related articles" function was used to broaden the sources. Moreover, reference articles of the relevant studies on this topic of interest were traced and checked to identify potential studies.

Bibliographic citation management EndNote software (Version X6, Thomson Corporation, Toronto, Canada) was used to manage the retrieved studies. The titles and abstracts of these studies were independently reviewed by 2 authors to identify potentially eligible studies. Subsequently, the full text of these potentially eligible studies was acquired and carefully evaluated by 2 independent authors through reading the full text, referring to the above inclusion and exclusion criteria. A group meeting was held to discuss and solve any disagreement during this process.

2.3. Data extraction and methodological quality assessment

Data were extracted by 2 authors independently. Any disagreement during this process was resolved by discussion among the authors. The following general information was extracted: first author, year of publication, country, number of patients in each group, patient characteristics, and study type. The outcome of interest included: prolonged ventilation, reintubation, pleural effusion, pneumothorax, pneumonia, respiratory failure, atrial fibrillation, myocardial infarction, stroke, renal failure, re-operation for bleeding, wound infection, mortality, length of intensive care unit (ICU) stay, and length of hospital stay.

Chronic renal failure (CRF) was defined as serum creatinine more than 2 mg/dL. Stroke was referred to cerebrovascular diseases, including intracranial hemorrhage, ischemia, and conditions that affect the blood circulation to the brain, leading to central neurologic deficit persisting for more than 72 hours. Urgent surgery was considered when there is a cardiac instability requiring care and performing surgery during the hospital stay. Emergent surgery was referred to as an acute clinical episode of coronary disease that requires surgery within hours. Prolonged ventilation was defined as the need for respiratory support for more than 10 hours. Postoperative mortality was defined as death occurring within 30 days postoperatively or at any time before discharge from the hospital.

The Jadad scale was used to assess randomized clinical trials (RCTs). There were 3 methodological items, including randomization (0–2 points), blinding (0–2 points), and dropouts and withdrawals (0–1 point). The quality scale ranges from 0 to 5 points. High-quality study was defined as study score not <3 points.

The Newcastle–Ottawa Scale (NOS) was used to evaluate the methodological quality of cohort studies. The main evaluated methodological items included the following: patient selection, comparability of cases, controls based on the study design or analysis, and outcomes. Because the NOS uses a star system, studies that scored more than 6 stars were considered to be of moderate to high quality.

2.4. Statistical analysis

Review Manager (The Cochrane Collaboration, Version 5.3, UK) was used for statistical analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for analyzing dichotomous data. For continuous data, mean difference (MDs) and 95% CIs were calculated. When continuous variables presented as medians with only ranges, the mean and standard deviation were estimated using the method reported by Hozo et al[13] Heterogeneity across studies was evaluated by the I^2 test. Study homogeneity was confirmed if the I^2 value $<50\%$ or $P>.1$, and the fixed effect model was used. Otherwise, the random effect model would be adopted. Funnel plots were adopted to assess the publication bias. Moreover, Begg and Egger tests were used to aid in interpreting the presence of publication bias by STATA software (Version 10.0, STATA Corporation, TX). Sensitivity analysis was used to analyze and evaluate the reliability of the

results. Sensitivity analysis was performed through omitting 1 study at a time to assess the effect of any individual study on the overall heterogeneity. Statistical significance was determined by $P < .05$.

2.5. Ethical approval

The present study was a meta-analysis that analyzed existing studies and did not need to handle individual patient data. Thus, ethical approval was unnecessary.

3. Results

3.1. Search results and study characteristics

Using the above search strategy, a total of 897 studies were obtained from the databases, and another 1 study was identified from the references. Among these studies, 214 duplicates were removed with Endnote software. Subsequently, 642 irrelevant studies were excluded by scanning the titles. The full texts of the remaining studies were reviewed, 3 conference and letters, 1 review, 2 studies with overlapped populations, 1 study with small sample size, 5 non-comparative studies, 2 studies with unavailable original data, 10 studies with irrelevant topic of interests, 5 studies with patients undergoing more than isolated CABG, and 5 studies with different spirometry criteria for COPD were excluded by referring to the inclusion and exclusion criteria. Finally, 8 studies were included in the present study.[8,10,14–19] A flow diagram for the searching and selection process is shown in Figure 1. This study enrolled 18,369 patients, with 3255 and 15,114 patients in the COPD and control groups, respectively. Table 1 shows the basic information of the included studies. The perioperative characteristics of patients and surgical procedures from the included studies are shown in Table 2.

3.2. Quality judgments of studies

The Jadad scale and the NOS were used to evaluate the quality of RCT and cohort study, respectively. All 8 cohort studies scored 6 or more stars, indicating moderate to high quality, whereas the quality of the RCT conducted by Starobin et al[15] was relatively low.

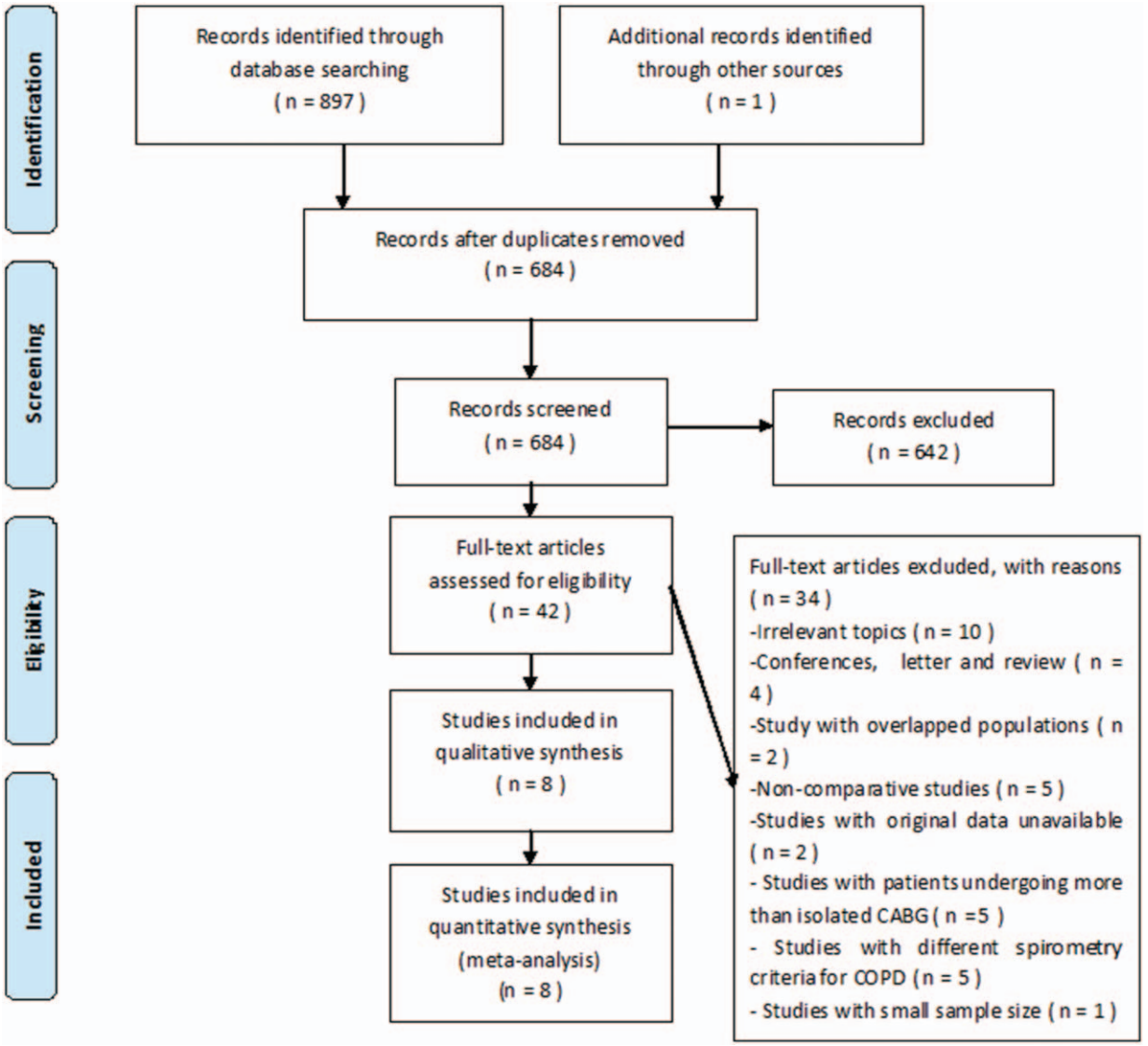

Figure 1. Flow diagram of the study.

Table 1

The basic information of the included trials.

First author, year	Country	Number of patients		Gender (Male/Female)		Age (year)		Study type	score
		COPD	Control	COPD	Control	COPD	Control		
Fuster et al, 2006	Spain	368	862	328/40	691/171*	64.9±8.3	62.4±9.7*	Retrospective cohort study	6‡
Manganas et al, 2007	Canada	221	101	172/49	77/24	68.1±7.1	67.5±8.2	Retrospective cohort study	7‡
Starobin et al, 2007	Israel	30	30	24/6	27/3	67.7±9.2	66.4±9.9	Randomized clinical trail	2†
Lizak et al, 2009	Poland	30	3449	26/4	2627/822	65±9	61±9*	Retrospective cohort study	6‡
Woods et al, 2010	USA	1739	8675	1217/522	6170/2505	64.6±9.9	64.3±10.8	Cohort study	8‡
Stelle et al, 2011	USA	56	124	41/15	80/44	66.6±11.4	62.3±10.3*	Retrospective cohort study	7‡
Najafi et al, 2015	Iran	105	461	72	351	58.2±8.4	59.3±9	Cohort study	8‡
Ho et al, 2016	Taiwan	706	1412	614/92	1228/184	NR	NR	Matched-pair cohort analysis	8‡

COPD = chronic obstructive pulmonary disease, USA = the United States of America.

* Significant difference.

† Randomized clinical trial (RCT), and the Jadad scale points.

‡ Cohort study, and the Newcastle–Ottawa Scale (NOS) score.

Table 2

Perioperative characteristics of patients and operations from the included studies.

First author, year	Somking history		Hypertension		Diabetes		Dyslipidemia		Ejection fraction (%)		Previous atrial fibrillation		Previous cerebrovascular accident		Chronic renal failure		Average number of grafts		Emergent/urgent operation	
	COPD	control	COPD	control	COPD	control	COPD	control	COPD	Control	COPD	control	COPD	control	COPD	control	COPD	Control	COPD	control
Fuster et al, 2006	NR	NR	196	415	125	298	190	491	53.9±13.4	56.4±11.8*	NR	NR	20	47	24	28*	2.9±1.0	3.1±1.0*	56	74*
Manganas et al, 2007	213	77*	69	25	55	28	NR	NR	NR	NR	15	6	NR	NR	22	4	3.4±1.0	3.6±1.0	34	21
Starobin et al, 2007	26	20	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3.1±0.9	2.9±0.8	NR	NR
Lizak et al, 2009	29	2373*	23	2517	8	989	19	1476*	NR	NR	1	173	0	197	2	173	2.6±1.3	2.7±0.9	NR	NR
Woods et al, 2010	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1.12±0.50	1.17±0.56	615	3042
Ho et al, 2016	NR	NR	439	881	278	556	157	309	NR	NR	NR	NR	99	195	NR	NR	NR	NR	NR	NR
Stelle et al, 2011	29	45	NR	NR	18	56	NR	NR	48.5±14.3	51.1±12.8	5	7	NR	NR	NR	NR	3.9±1.0	4.1±1.2	30	65
Najafi et al, 2015	36	167	59	220	45	187	81	317	48.4±10.3	48.5±10.3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

COPD = chronic obstructive pulmonary disease.

* Significant difference.

3.3. Postoperative results

Postoperative mortality was reported in 5 studies, with 3064 and 14499 patients in the COPD group and control groups, respectively.[8,10,14,16,17] The pooled analysis showed that the mortality rates were similar between the 2 groups (Table 3). Because the data on the number of deaths for each specified reason was unavailable from parts of the included studies, further analysis on mortality could not be conducted in the present study.

Data on prolonged ventilation were available in 4 studies, including 2384 and 9762 patients in the COPD and control

Table 3

Summary of meta-analysis.

Outcome of interest	Statistical method	Number of studies	MD/OR	95% CI	*P* value	Heterogeneity	
						P	I^2
Mortality3064/14499	Random	5	1.62	0.66, 3.99	.29	<.00001**	90%
Prolonged ventilation2384/9762	Random	4	1.69	0.82, 3.49	.16	.01*	73%
Reintubation619/4412	Random	3	2.40	0.63, 9.09	.20	.11	55%
Pleural effusion281/3580	Fixed	3	2.36	0.85, 6.55	.10	.18	42%
Pneumothorax281/3580	Fixed	3	1.90	0.75, 4.83	.18	.93	0%
Pneumonia3428/17058	Fixed	7	2.92	2.37, 3.60	<.00001**	.73	0%
Respiratory failure1487/5170	Random	4	4.01	1.19, 13.51	.03*	<.0001**	87%
Atrial fibrillation675/4536	Fixed	4	1.10	0.84, 1.43	.50	.81	0%
Myocardial infarction	Random	3	0.70	0.58, 0.85	.0004**	.0003**	88%
Stroke484/4465	Fixed	4	2.91	1.37, 6.18	.005**	.60	0%
Renal failure2193/13110	Fixed	4	1.60	1.30, 1.97	<.00001**	.19	37%
Re-operation for bleeding2163/9661	Fixed	3	1.13	0.78, 1.64	.51	.74	0%
Wound infection1874/9166	Fixed	3	2.16	1.21, 3.88	.01*	.53	0%
Length of ICU stay2384/9762	Fixed	4	−0.04 days	−0.10, 0.02	.19	.16	42%
Length of hospital stay3090/11174	Random	5	0.79 days	−0.03, 1.61	.06	<.00001**	98%

CI = confidence interval, ICU = intensive care unit, MD = mean difference, OR = odds ratio.

* Significant difference, $P<.05$.

** Significant difference, $P<.01$.

groups, respectively.[10,14,17,18] However, no significant difference was found between the 2 groups in terms of prolonged ventilation (OR = 1.69; 95% CI: 0.82–3.49, $P = .16$; $P = .01$ for heterogeneity) (Table 3). With regard to reintubation, data from 3 studies with 5021 patients were available.[10,14,16] A pooled analysis was conducted showing no significant difference between the 2 groups (OR = 2.40; 95% CI: 0.63–9.09, $P = .20$; $P = .11$ for heterogeneity) (Table 3). 3 studies reported pleural effusion, with 281 and 3580 patients in the COPD and control groups, respectively.[10,15,16] After pooling the effects, no significant difference was found concerning pleural effusion between the 2 groups (OR = 2.36; 95% CI: 0.85–6.55, $P = .10$; $P = .18$ for heterogeneity) (Table 3). Data on pneumothorax were reported in 3 studies, including 3861 patients.[10,15,16] The pooled analysis showed that the pneumothorax rates were also similar between the 2 groups (OR = 1.90; 95% CI: 0.75–4.83, $P = .18$; $P = .93$ for heterogeneity) (Table 3). With regard to pneumonia, 7 studies included 3428 and 17,058 patients in the COPD and control groups, respectively.[8,10,14–18] The pooled analysis showed that the pneumonia rate in the COPD group was significantly higher than that in the control group OR = 2.92; 95% CI: 2.37 to 3.60, $P < .00001$; $P = .73$ for heterogeneity) (Table 3). Data on respiratory failure were reported in 4 studies, with 1487 and 5170 patients in the COPD and control groups, respectively.[8,14,15,19] The pooled analysis showed that the respiratory failure rate in the COPD group was significantly higher than that in the control group (OR = 4.01; 95% CI: 1.19–13.51, $P = .03$; $P < .001$ for heterogeneity) (Table 3).

Postoperative complications other than pulmonary-related items including atrial fibrillation, myocardial infarction, stroke, renal failure, re-operation for bleeding, and wound infection were also analyzed in the present study. 4 studies compared atrial fibrillation, with 675 and 4536 patients in the COPD and control groups, respectively.[10,14,16,18] There seemed to be no significant difference in atrial fibrillation between the 2 groups (OR = 1.10; 95% CI: 0.84–1.43, $P = .50$; $P = .81$ for heterogeneity) (Table 3). Three studies, involving 3914 patients, reported myocardial infarction.[8,14,19] The pooled analysis indicated a significant lower myocardial infarction rate in the COPD group than the control group rate (OR = 0.70; 95% CI: 0.58–0.85, $P = .0004$; $P = .0003$ for heterogeneity) (Table 3). Stroke was reported in 4 studies involving 4949 patients, with 484 and 4465 patients in the COPD and control groups, respectively.[14–16,18] The pooled analysis showed that the stroke rate in the control group was significantly lower than that in the COPD group after CABG (OR = 2.91; 95% CI: 1.37–6.18, $P = .005$; $P = .60$ for heterogeneity) (Table 3). With regard to renal failure, 4 studies involving 15303 patients were included.[14,16–18] The renal failure rate in the control group was also significantly lower than that in the COPD group (OR = 1.60; 95% CI: 1.30–1.97, $P < .00001$; $P = .19$ for heterogeneity) (Table 3). 3 studies involving 11824 patients reported the number of re-operations for bleeding.[14,17,18] No significant difference was found in the re-operation rate for bleeding between the 2 groups (OR = 1.13; 95% CI: 0.78–1.64, $P = .51$; $P = .74$ for heterogeneity) (Table 3). Wound infection was reported in 3 studies with 1874 and 9166 patients in the COPD and control groups, respectively.[15,17,19] The pooled analysis showed that the wound infection rate in the COPD group was significantly higher than that in the control group after CABG (OR = 2.16; 95% CI: 1.21–3.88, $P = .01$; $P = .53$ for heterogeneity).

The length of ICU stay was reported in 4 studies involving 12146 patients, with 2384 and 9762 patients in the COPD and control groups, respectively.[10,14,17,18] No significant difference in was found in the length of ICU stay between the 2 groups (MD = −0.04 days; 95% CI: −0.10 to 0.02, $P = .19$; $P = .16$ for heterogeneity) (Table 3). With regard to the length of hospital stay, data from 5 studies with 14,264 patients were available.[8,10,14,17,18] The pooled analysis showed that the length of hospital stay in the COPD group was significantly longer than that in the control groups (MD = 0.79 days; 95% CI: −0.03 to 1.61, $P = .06$; $P < .00001$ for heterogeneity) (Table 3).

3.4. Sensitivity analysis

Sensitivity analysis was performed because significant heterogeneity was observed in mortality, prolonged ventilation, reintubation, respiratory failure, myocardial infarction, and length of hospital stay.

For mortality and myocardial infarction, heterogeneity remained high, and the pooled result remained unchanged while performing the sensitivity analysis. With regard to prolonged ventilation, high heterogeneity existed consistently while performing the sensitivity analysis. After removing the study by Manganas et al[10] sensitivity analysis showed that prolonged ventilation rate was significantly higher in the COPD group (OR = 2.37; 95% CI: 1.37–4.12, $P = .002$; $P = .12$, $I^2 = 53\%$ for heterogeneity). With regard to reintubation, heterogeneity disappeared when the study by Fuster et al was removed.[14] Sensitivity analysis found that reintubation rate became significantly higher in the COPD group after the study by Manganas et al was removed (OR = 4.67; 95% CI: 1.94–11.22, $P = .0006$; $P = .18$, I2 = 45% for heterogeneity).[10] For respiratory failure, the heterogeneity disappeared when the study by Najafi et al[19] was removed, and the pooled results changed into no significant difference between the 2 groups while removing the study by Ho et al (OR = 4.00; 95% CI: 0.63–25.40, $P = .14$; $P = .003$, $I^2 = 83\%$ for heterogeneity).[8] The heterogeneity in length of hospital stay remained high while performing the sensitivity analysis. The length of hospital stay rate became significantly higher in the COPD groups after removing the study by the Stelle et al (MD = 1.02 days; 95% CI: 0.08–1.96, $P = .03$; $P < .00001$, I2 = 97% for heterogeneity).[18]

3.5. Publication bias

Funnel plot analysis was performed for pneumonia, respiratory failure, myocardial infarction, stroke, renal failure and wound infection. The funnel plot for pneumonia, stroke, renal failure, and wound infection between the COPD and control groups showed a symmetrical distribution of the included studies on both sides of the vertical line, which indicated no serious publication bias (Fig. 2A, Fig. 2D, Fig. 2E, and Fig. 2F). Because high heterogeneity existed in the analysis of respiratory failure, both Begg and Egger tests, as well as the funnel plot, were used to detect publication bias. The funnel plot on respiratory failure showed that 2 studies were in the non-significant areas, and the other 2 studies were in significant areas, indicating publication bias (Fig. 2B). However, the Begg and Egger tests showed there was no publication bias, with $P = 1.000$ and $P = .338$ for the Begg and Egger tests, respectively. With regard to myocardial infarction, the funnel plot showed that one study was in the non-significant areas, and the other 2 studies were in the significant areas (Fig. 2C). All studies investigating myocardial infarction yielded $P = 1.000$ and $P = .179$ in Begg and Egger tests, respectively. Although scores of both Begg and Egger tests on

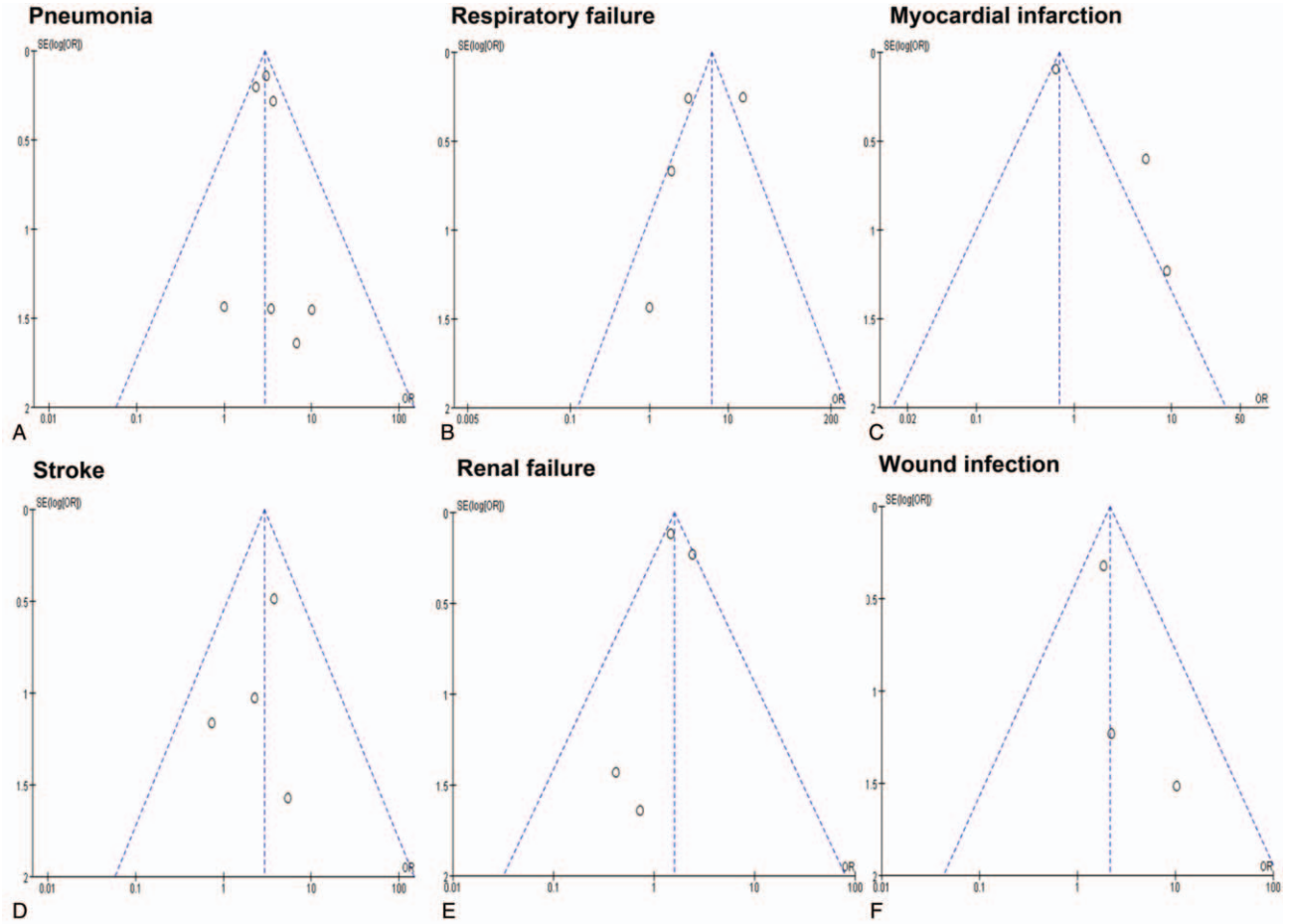

Figure 2. Funnel plot for results from included studies comparing postoperative outcomes between patients with and without COPD. A. Funnel plot of pneumonia. B. Funnel plot of respiratory failure. C. Funnel plot of myocardial infarction. D. Funnel plot of stroke. E. Funnel plot of renal failure. F. Funnel plot of wound infection. COPD = chronic obstructive pulmonary disease.

respiratory failure and myocardial infarction showed no publication bias, these results could be limited by the small number of the studies included for these 2 items.

4. Discussion

COPD is characterized by a persistent airflow limitation and a remodeling of small airways.[2] In the lung of COPD patient, the chronic hypoxia-induced by airflow limitation increases the activity of angiotensin-converting enzyme (ACE), which may further negatively affect the peripheral use of oxygen and respiratory muscle function. The activation of renin-angiotensin system (RAS) could lead to cell proliferation, hypertrophy, vasoconstriction, and inflammation of the pulmonary vasculature. Moreover, aldosterone was reported to have similar effect on the pulmonary vascular network, as it binds to mineralocorticoid receptors promoting signaling pathways that contribute to vascular remodeling.[20,21] Among the pathological lung tissue remodeling mentioned in the introduction part, inflammation could contribute to angiogenesis through inducing the inflammatory cells as well as through increasing the level of angiogenetic mediators. Angiogenesis together with inflammation play an important part in remodeling of airways, which may contribute to adverse effects on various extrapulmonary organs in COPD patients[3,4] Thus, the impact of severe lung disease such as COPD on patients undergoing cardiac surgery was traditionally considered potentially dangerous for cardiac surgery. With regard to patients undergoing CABG, COPD was reported to be an independent risk factor for postoperative morbidity and/or mortality.[7,22] However, because of the recent improvements in anesthesia, cardiac protection, and surgical techniques, as well as the advances in preoperative pulmonary evaluation and medical optimization, it becomes possible to perform CABG with acceptable morbidity and mortality rates in patients with high-risk. More and more studies have reported that patients with mild to moderate COPD or even COPD did not have a higher risk of postoperative mortality and morbidity rates than those without COPD.[9,11,23] However, a recent Chinese study still suggested COPD to be an independent risk factor for postoperative mortality after CABG.[24] To further clarify this divergence, the present meta-analysis on this topic of interest was performed.

Data on the perioperative results and mortality outcomes from the relevant studies were reviewed and synthesized. The definition of COPD in published studies was not unified. Patients with diverse spirometry values were considered as COPD in these published studies. In the present study, to reduce the potential bias in the COPD definition, only studies with COPD confirmed by a FEV1/FVC lower than 70%, or by the diagnosis and/or treatment record were included. Studies with COPD confirmed by only a FEV1 <75% of the predicted value or so were excluded.

One of the main findings of the present study was that COPD was not associated with an increased risk of postoperative mortality for patients undergoing CABG. Although the result was contradicted to those previously reported in some studies, other studies have also failed to identify COPD as independent risk factor for postoperative mortality after CABG.[25,26] The study conducted by Ried et al reported a mortality rate of 6.1% for COPD patients, which was significantly higher than the 0.8% for patients without COPD after cardiac surgery.[25] Some other studies found that mild-to-moderate COPD did not increase postoperative mortality, with only severe COPD contributing to worse outcome.[9,26] In the study by Angouras et al, propensity-matched analysis was performed, and no difference in mortality was found between patients with and those without COPD.[11] Further subgroup analysis of mortality based on the severity of COPD was supposed to be performed in the present study. However, only 3 of the included studies stratified patients with COPD into subgroups, and the criteria for the severity level of lung function were different across these studies. Therefore, the present meta-analysis study was unable to conduct a subgroup analysis on mild-to-moderate and severe COPD. On the basis of the contents of some included studies, most enrolled patients had mild-to-moderate COPD.[10,14,15,18,19] Furthermore, there might be a selection of patients with COPD by surgeons when CABGs were performed in these studies, for patients with mild-to-moderate COPD were at lower risk compared with those with severe COPD. Because most included studies were published in the last decade, another potential explanation may be attributed to the recent improvements in anesthesia, cardiac protection, and surgical techniques. This could be more prominent in the included study conducted by Manganas et al[10] with no postoperative mortality found in patients with severe COPD. Thus, this result of the present study indicated that CABG was generally safe for patients with COPD under the current medical condition.

Considering pulmonary-related morbidity, the present study found that COPD increased the risk of postoperative pneumonia and respiratory failure. This result was in agreement with the study conducted by Ried et al[27] In the study by Samuels et al[9] the pneumonia rate was also found to be more prominent for patients with COPD after cardiac surgery. The underlying mechanism may be that patients with COPD usually develop a differential inflammatory response with increased release of cysteinyl leukotrienes during cardiac surgery, which could lead to potential small airway dysfunction.[28] Meanwhile, various proinflammatory mediators produced during this process combined with the respiratory muscle dysfunction caused by anesthesia and surgery, could lead to atelectasis in the basal lung segments and compromising the gas exchange.[29] All of these changes may predispose patients to pulmonary infection and increase the risk of pulmonary dysfunction, and even respiratory failure.[30,31] Thus, patients with COPD may be unable to tolerate further reduction in lung function after CABG and would likely develop more pulmonary complications.

Considering non-pulmonary morbidities, postoperative stroke and renal failure were more frequent among patients with COPD in the present study. These results were in agreement with the study conducted by Efird et al, in which patients with COPD were also found to present with a higher rate of renal failure and stroke than patients without COPD.[27] Rodrigues et al also confirmed that COPD was an independent risk factor for renal failure after cardiac surgery.[32] Another significant difference between patients with and those without COPD was found in terms of wound infection. COPD was found to be significantly associated with wound infection in the present study. In the study conducted by Meszaros et al, COPD was also reported to be an independent predictor of sternal wound infection.[33]

As is known, COPD patients present with airflow limitation. Myocardial ischemia is associated with the imbalance between oxygen transport and necessity. The surgical stress increases the myocardial oxygen need, which may deteriorate the balance between oxygen transport and necessity causing postoperative myocardial infarction. However, the present study showed that COPD was associated with lower risk of postoperative myocardial infarction after CABG. The data from the study conducted by Ho et al involving 2118 patients mainly affected this pooled analysis.[8] The study by Ho et al. reported a significantly higher rate of postoperative myocardial infarction for patients without COPD after propensity score matching, which was in contrast with the results from the other 2 studies.[8,14,19] Moreover, the incidence rates of postoperative myocardial infarction in the study by Ho et al were 35.91% for patients without COPD and 26.63% for patients with COPD.[8] In the other 2 studies, the incidence rates of postoperative myocardial infarction range between 0.3% and 2.4%.[14,19] Thus, other factors may affect the incidence rate of postoperative myocardial infarction in the study by Ho et al, such as perioperative medication, surgical techniques, and medical capabilities of the medical centers involved in the investigated database. The result of myocardial infarction in the present study was in contrast with that reported by Efird et al's study in which no significant difference was found on postoperative myocardial infarction rates between patients with and without COPD.[27] Although scores of both Begg and Egger tests on myocardial infarction showed no publication bias, this results could be limited by the small number of the studies included. Moreover, according to the funnel plot analysis, 1 study was in the non-significant areas. Therefore, better quality-designed studies concerning postoperative myocardial infarction after CABG for patients with COPD are still needed.

Another interesting finding of our study is the incidence of postoperative atrial fibrillation was similar between patients with and without COPD. This result was in contrast with the study conducted by Samuels et al[9] Usually, studies showed that COPD was an independent risk factor for atrial fibrillation.[34,35] The reason for the present study may be partly attributed to the application of early prophylactic treatment which significantly reduced the occurrence of supraventricular arrhythmia in the study conducted by Fuster et al[14] The not prominent rate of atrial arrhythmia for patients with COPD might have contributed to the similar mortality rates between the 2 groups.

Some limitations should be considered when interpreting the results in the present study. First, most of the included studies were cohort studies, and publication bias cannot be avoided because of its nature. Besides, only one of the included studies was an RCT, but its methodological quality was relatively low. These above facts could negatively affect the reliability and validity of the present meta-analysis. Second, indirect data acquisition methods were employed when calculating data based on the continuous variables presented as medians with ranges.[13] Third, because no internationally unified criteria existed until recently, the definition of COPD in published studies was various. In the present study, only studies with COPD confirmed by a FEV1/FVC lower than 70%, or by the diagnosis and/or treatment record were included. Although these inclusion criteria were aimed to reduce the potential bias in the COPD definition, it

might also induce bias in the results to some extent. Four, the included studies cover a relatively long period, during which variable changes may occur in the operative and postoperative practices. These changes might affect the outcomes of interest. Five, although all the included cohort studies were of moderate to high quality, the baseline characteristics for some studies were not comparable between patients with and without COPD. For example, in the study conducted by Fuster et al[14] differences were found in terms of preoperative gender, age, and so on. Because parts of these preoperative items are associated with the postoperative mortality and morbidity for patients undergoing CABG, these could also affect the results to some extent.[36] Thus, the results of the present study should be cautiously interpreted.

5. Conclusion

To the best of our knowledge, this is the first meta-analysis to date focusing on the postoperative outcomes following CABG for patients with COPD. In the present study, COPD was not associated with a higher risk of postoperative mortality following CABG. However, the present study indicated that patients with COPD were at higher risks for developing postoperative morbidities, particularly pneumonia, respiratory failure, stroke, renal failure, and wound infection. Thus, cautions should be taken when a patient with COPD is indicated for CABG, considering the higher odds of postoperative complications involving the respiratory system and others. Better quality designed RCTs are still needed to confirm our results.

Author contributions

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