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<th>Chronic obstructive pulmonary disease: An independent risk factor for long-term cardiac and cardiovascular mortality in patients with ischemic heart disease</th>
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<td>Author(s)</td>
<td>Nishiyama, Kei; Morimoto, Takeshi; Furukawa, Yutaka; Nakagawa, Yoshihisa; Ehara, Natsuhiko; Taniguchi, Ryouji; Ozasa, Neiko; Saito, Naritatsu; Hoshino, Kozo; Touma, Masanao; Tamura, Toshihiro; Haruna, Yoshisumi; Shizuta, Satoshi; Doi, Takahiro; Fukushima, Masanori; Kita, Toru; Kimura, Takeshi</td>
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Kyoto University
Abstract: Background:
Limited data are available on long-term mortality and morbidity of patients with chronic obstructive pulmonary disease (COPD) and ischemic heart disease. We examined how COPD affects the long-term mortality and morbidity after undergoing percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG).

Methods:
We analyzed 9877 consecutive patients who underwent their first elective PCI ($n = 6878$) and CABG ($n = 2999$) in 2000-2002 at 30 institutions listed in the CREDO-Kyoto registry.

Results:
COPD was diagnosed in 240 patients (2.4%). In-hospital mortality (1.3% vs. 1.2%, \( p = 0.972 \)) did not differ between patients with and without COPD. During long-term follow up (42.8 months), 906 patients (9.4%) died, 517 (5.3%) of whom died of cardiovascular death and 376 (3.9%), of cardiac death. At 3 years, the unadjusted survival rate and the rates of freedom from cardiovascular death and cardiac death were 92.1%, 95.3%, and 96.5% in the total population and 82.8%, 91.7%, and 92.1% in patients with COPD respectively. Log-rank test indicated that COPD was associated with higher incidence of all-cause mortality (\( p < 0.0001 \)), cardiovascular death (\( p = 0.0002 \)), and cardiac death (\( p < 0.0001 \)). Multivariate analyses indicated that COPD was an independent predictor of all-cause mortality (hazard ratio 1.36, \( p = 0.0003 \)), cardiovascular death (hazard ratio 1.28, \( p = 0.0407 \)), and cardiac death (hazard ratio 1.48, \( p = 0.003 \)).

Conclusions:
COPD is an independent risk factor for long-term cardiac and cardiovascular mortality in patients with ischemic heart disease.

Suggested Reviewers:
Chronic Obstructive Pulmonary Disease—an Independent Risk Factor for Long-term Cardiac and Cardiovascular Mortality in Patients with Ischemic Heart Disease

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Key words:

Chronic obstructive pulmonary disease, Ischemic heart disease, prognosis, Cardiac death, Cardiovascular death

All authors have read and approved the manuscript. No conflicts of interest exist among any of the authors in this study.

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Structured abstract (Word count = 248)

Background:

Limited data are available on long-term mortality and morbidity of patients with chronic obstructive pulmonary disease (COPD) and ischemic heart disease. We examined how COPD affects the long-term mortality and morbidity after undergoing percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG).

Methods:

We analyzed 9877 consecutive patients who underwent their first elective PCI (n = 6878) and CABG (n = 2999) in 2000–2002 at 30 institutions listed in the CREDO-Kyoto registry.

Results:

COPD was diagnosed in 240 patients (2.4%). In-hospital mortality (1.3% vs. 1.2%, p = 0.972) did not differ between patients with and without COPD. During long-term follow-up (42.8 months), 906 patients (9.4%) died, 517 (5.3%) of whom died of cardiovascular death and 376 (3.9%), of cardiac death. At 3 years, the unadjusted survival rate and the rates of freedom from cardiovascular death and cardiac death were 92.1%, 95.3%, and 96.5% in the total population and 82.8%, 91.7%, and 92.1% in patients with COPD respectively. Log-rank test indicated that COPD was associated with higher incidence of
all-cause mortality (p < 0.0001), cardiovascular death (p = 0.0002), and cardiac death (p < 0.0001). Multivariate analyses indicated that COPD was an independent predictor of all-cause mortality (hazard ratio 1.36, p = 0.0003), cardiovascular death (hazard ratio 1.28, p = 0.0407), and cardiac death (hazard ratio 1.48, p = 0.003).

Conclusions:

COPD is an independent risk factor for long-term cardiac and cardiovascular mortality in patients with ischemic heart disease.
Chronic obstructive pulmonary disease (COPD) is a common comorbidity among patients undergoing percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) \(^1\)-\(^3\). Although some cohort studies have revealed that patients with COPD have a significantly higher risk of in-hospital mortality and long-term all-cause mortality following PCI and CABG \(^4\)-\(^14\), the effects of COPD on long-term mortality and morbidity in patients with ischemic heart disease have not been adequately demonstrated. To examine these effects, we evaluated the long-term outcomes of patients undergoing coronary revascularization in a large-scale multicenter registry in Japan.
**Materials and methods**

The Coronary Revascularization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) registry has collected data on the potential risk factors and outcomes in 9877 consecutive patients who underwent their first elective PCI (n = 6878) and CABG (n = 2999) at the 30 institutions between 2000 and 2002 in Japan. Patients with acute myocardial infarction within 1 week prior to the index procedure were excluded. The relevant review boards or ethics committees in all 30 participating centers (Appendix A) approved the research protocol. A description of the design and study protocol has been previously published\(^\text{15}\) and the study protocol is concordant with the guidelines for epidemiologic studies issued by the Ministry of Health, Labor and Welfare of Japan. In order to examine whether COPD is an independent predictor of all-cause mortality, cardiovascular death, and cardiac death following PCI and CABG, we performed post hoc analysis of the data collected from 9756 consecutive patients who survived their first elective PCI (n = 6846) and CABG (n = 2910). The primary end point was all-cause mortality, cardiovascular death, and cardiac death. Demographic and angiographic characteristics before coronary intervention, and procedural data were collected from hospital charts or databases in each center by independent clinical research coordinators (Appendix B) according to prespecified definitions. Data in this
registry include patient demographics (e.g., age and gender), potential risk factors, and comorbidities (e.g., COPD, stroke, hypertension, and current smoking status) that have been demonstrated to be related to short-term and long-term outcomes.

All procedural decisions, including the technique of revascularization and device selection, were made at the discretion of the patient, the physician, and the surgeon performing PCI and CABG.

**Definition**

A patient was considered to have COPD if it was listed as a comorbid condition in our database and its diagnosis was confirmed by a simple test called spirometry, which measures how deeply a person can breathe and how fast air can move into and out of his or her lungs. Such a diagnosis should be considered in any patient who has symptoms of cough, sputum production, or dyspnea (difficult or labored breathing), and/or a history of exposure to risk factors for the disease. In cases where spirometry is unavailable, the diagnosis of COPD should be made using all available tools. Clinical symptoms and signs such as abnormal shortness of breath and increased forced expiratory time can be used to arrive at the diagnosis. A low peak flow is consistent with but not specific to COPD because it can be caused by other lung diseases and by poor
performance during testing. Chronic cough and sputum production often precede the development of airflow limitation by many years, although not all individuals with cough and sputum production go on to develop COPD. Congestive heart failure was diagnosed on the basis of clinical signs (New York Heart Association [NYHA] ≥ II). Diabetes or hypertension was considered to be present if the patients were previously diagnosed by another physician or if they were being treated with either insulin or oral antidiabetic drugs, or antihypertensive drugs respectively. Patients were considered to have a history of myocardial infarction if previously diagnosed by electrocardiogram or coronary angiography. The criteria for the diagnosis of periprocedural myocardial infarction were the appearance of new Q waves and an increase in creatine kinase to ≥2.0 times the upper limit of normal occurring ≤24 hours after PCI. Stroke at the baseline included asymptomatic stroke detected by non-invasive imaging modalities. Peripheral vascular disease was considered to be present when patients were being treated for carotid, aortic, and/or other peripheral vascular diseases or were scheduled for surgical or endovascular interventions. Left ventricular ejection fraction was measured either by contrast left ventriculography or echocardiography. Patients with left ventricular ejection fraction ≤40% were deemed to have left ventricular dysfunction. Chronic renal disease was identified when the creatinine clearance estimated by
Cockroft-Gault formula was less than 60 mL/min. Anemia was defined as blood hemoglobin level < 12 g/dL.

Long-term follow up was performed using outpatient visits and chart review. A central adjudication committee reviewed all deaths in a blinded fashion by using source documentation provided by the site investigators.

**Statistical analysis**

Standard descriptive statistics (proportions and 2 tests) were used to list patient and disease characteristics by subgroup. Statistical analysis of categorical variables was carried out using cross tables with the Pearson $\chi^2$ test. Survival curves were estimated using the Kaplan-Meier method and compared with the log-rank statistics. To determine the baseline risk factors for the incidence of all-cause mortality, cardiovascular death, and cardiac death, we developed Cox proportional hazards models for the following 24 potential variables: COPD, the technique of revascularization, gender, body mass index, emergency procedure, prior myocardial infarction, congestive heart failure, stroke, peripheral artery disease, chronic atrial fibrillation, malignancy, hypertension, diabetes without insulin therapy, diabetes with insulin therapy, dialysis, chronic renal disease, anemia, current smoking status, left ventricular dysfunction, chronic total occlusion of
the coronary artery, proximal left anterior descending coronary artery disease, left main coronary artery disease, age, and triple vessel disease. All continuous variables were dichotomized so as to agree with the proportional assumptions according to the predetermined clinical contexts. We plotted log (time) vs. log[–log (survival)] stratified by each significant risk factor and evaluated whether the plotted lines were parallel\(^{16}\). The variables for which \(p\) values were less than 0.05 in univariate analyses and proportional assumptions were generally fair were included in the multivariate analyses. We developed multivariate Cox proportional hazards models that controlled for significant risk factors while testing for significant differences in long-term results. The appropriateness of the proportional hazards assumption for these variables has been attested elsewhere (Kimura manuscript). All analyses were performed with JUMP version 6.0.3 (SAS; Cary, NC).
Results

COPD was diagnosed in 240 patients (2.4%) on the basis of the baseline characteristics, which are shown in Table 1. Patients with COPD were more likely to have congestive heart failure, stroke, peripheral artery disease, chronic renal disease, anemia, and left ventricular dysfunction. They also tended to be older and had a lower average body mass index. Patients without COPD were more likely to be women and having diabetes that did not require insulin therapy. No difference was detected in the current smoking status in the 2 groups.

In-hospital mortality (1.3% vs. 1.2%, p = 0.9724) and in-hospital Q-wave myocardial infarction incidence (0.8% vs. 0.9%, p = 0.8572) did not differ between the groups (Table 2).

A total of 98% and 95% patients continued to attend follow-up examinations at the end of 1 and 2 years respectively. During long-term follow up (median follow-up period = 42.8 months), 906 patients (9.4%) died, 517 (5.3%) of which died of cardiovascular death and 376 (3.9%), of cardiac death. Of the total population, 265 patients (2.7%) suffered acute myocardial infarction, and 468 (4.8%) suffered stroke. Of the patients with COPD, 50 (21.3%) died, of which 24 (10.3%) died of cardiovascular death, and 22 (9.4%), of cardiac death. A total of 6 COPD patients (2.6%) suffered acute
myocardial infarction, and 11 (4.7%) suffered stroke. At 3 years, the unadjusted survival rate and the rates of freedom from cardiovascular death and cardiac death were 92.1%, 95.3%, and 96.5% in the total population and 82.8%, 91.7%, and 92.1% in patients with COPD, respectively.

Univariate analysis revealed that COPD was associated with higher all-cause mortality (p < 0.0001), cardiovascular death (p = 0.0002), and cardiac death (p < 0.0001); Kaplan-Meier survival curves are presented in Figure 1.

Multivariate analyses (considering the baseline characteristics and the results of univariate analyses) indicated that COPD was an independent predictor of all-cause mortality, cardiovascular death, and cardiac death after PCI and CABG (Table 3).
**Discussion**

Smoking as a risk factor is common to both COPD and ischemic heart disease; hence, these 2 diseases often coexist. Previous studies have shown that patients with COPD have a significantly higher risk of long-term all-cause mortality after PCI and CABG. The manner in which COPD affects long-term mortality and morbidity in patients with ischemic heart disease remains unresolved. We analyzed 9877 consecutive patients who underwent their first elective PCI (n = 6878) and CABG (n = 2999) at 30 institutions in Japan. Univariate and multivariate analyses in this study indicated that COPD was an independent predictor of all-cause mortality. To our knowledge, this study is the first to show that patients with COPD have a significantly higher risk of cardiac and cardiovascular death following PCI and CABG.

The manner in which COPD affects the incidence of long-term adverse cardiac events after coronary revascularization is not quite clear. It was reported that patients affected by COPD have an increased risk of acute atherothrombotic events, and that this increase is independent of smoking and other cardiovascular risk factors. Further, bronchial inflammation reportedly spreads to the systemic circulation and is known to play a key role in plaque formation and rupture. While the current smoking status did not differ between patients with and without COPD, this study reported that patients...
with COPD were more likely to have peripheral artery disease and stroke as pre-operative comorbidities. Exacerbation of COPD may overtax an already diseased heart because of hypoxemia and increased work of breathing. It was reported that severe hypoxemia can worsen cardiac ischemia in patients with ischemic heart disease \(^{20,21}\). On the other hand, exacerbation of ischemic heart disease can further impair gas exchange by incrementally increasing airway resistance or reducing mixed venous oxyhemoglobin saturation. Cardiac arrhythmias are frequent among patients with COPD. Previous studies reported widely various incidence of arrhythmia and arrhythmia related death in patients with COPD and it was reported that about ten percent of patients with COPD suffer from SCD \(^{22-26}\). However, the role of serious ventricular arrhythmias in these situations is unknown \(^{27}\). An association between severe COPD and increased QTc dispersion was reported, which has been reported as a marker of ventricular electrical instability \(^{28}\). It is not clear whether treating asymptomatic ventricular arrhythmia can reduce the incidence of SCD or not in patients with COPD \(^{22-26}\). This study demonstrated that COPD was associated with a higher incidence of long-term cardiac and cardiovascular mortality and morbidity. However additional interventional therapy for COPD was not recorded in our database, and so further study may be needed to investigate whether intervention for COPD can improve long-term
mortality and morbidity from cardiac causes in patients with ischemic heart disease.

Though it was reported that the severity of COPD might affect in-hospital outcomes after PCI and CABG, we found that patients with COPD undergoing elective PCI and CABG had in-hospital morbidity and mortality rates comparable with those of controls after first elective PCI and CABG in this study. Previously it was demonstrated that post-CABG mortality was largely higher in patients with severe COPD receiving steroids than that of patients without COPD, however post-CABG mortality of patients with mild or moderate COPD was similar to that of patients without COPD4, 5. However the severity of COPD was not well examined because pulmonary function test was not recorded in our database, and so further study may be needed to investigate the relationship between severity of COPD and short- and long-term mortality in patients with ischemic heart disease.

This study has some limitations. The definition of COPD in our study was consistent with that in many other studies1, 2, 9-11, and 240 patients with COPD were identified in our study, which accounted for 2.4% of total population. However, the definition of COPD might be slightly lenient because the results of pulmonary function tests were not recorded in our database. Because ventricular function was evaluated before PCI or CABG, substantial recovery of ventricular function may have occurred in
some patients with left ventricle dysfunction with a concomitant decrease in the risk of all-cause mortality and cardiac death. In this study, we found that after the first elective PCI and CABG, the in-hospital morbidity rates in patients with COPD and control were comparable. It has been reported that the severity of COPD might affect in-hospital outcomes after PCI and CABG \(^4,5\); however, the severity of COPD was not adequately determined in our study because the results of pulmonary function tests were not recorded in our database. Moreover, we have no information regarding the adjunctive pharmacotherapy after discharge and the duration of some of these comorbidities; these parameters may influence long-term mortality and morbidity.
Acknowledgments

We are indebted to the clinical research coordinators for data collection and to Miss Yoko Kasakura for secretarial assistance.
References


6. Canver CC, Nichols RD, Kroncke GM. Influence of age-specific lung function


10. van Domburg RT, Takkenberg JJ, van Herwerden LA, Venema AC, Bogers AJ.


and significance of cardiac arrhythmias in chronic obstructive lung disease. 

Predicting mortality of patients hospitalized for acutely exacerbated chronic 

respiratory failure in patients with chronic airway obstruction. Chest 

27. Burrows B, Earle RH. Course and prognosis of chronic obstructive lung disease. 

Effect of blood gas derangement on QTc dispersion in severe chronic obstructive 
pulmonary disease: evidence of an electropathy? Int J Cardiol 
**Figure legend**

Unadjusted Kaplan-Meier Event-free Survival Curves for All-cause Mortality (Panel A), Cardiovascular death (Panel B), and Cardiac Death (Panel C).

COPD = chronic obstructive pulmonary disease
### Appendices

#### Appendix A. List of participating centers and investigators

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<tr>
<th>Centers</th>
<th>Investigators</th>
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<td>Kazuaki Kataoka</td>
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<td>Japanese Red Cross Society, Wakayama Medical Center</td>
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Shuichi Hamasaki
Hiroyuki Yamamoto

Kansai Denryoku Hospital
Takeshi Aoyama
Takahiro Sakurai

Kishiwada City Hospital
Mitsuo Matsuda
Masahiko Onoe
Yuzo Takeuchi

Kitano Hospital
Ryuji Nohara
Kimisato Nakano

Kobe City Medical Center General Hospital
Shigefumi Morioka
Yukikatsu Okada
Kenichi Shiratori
Nasu Michihiro

Kokura Memorial Hospital
Masakiyo Nobuyoshi
Hitoshi Okabayashi
Hitoshi Yasumoto
Jyota Nakano

Koto Memorial Hospital
Tomoyuki Murakami
Katsuya Ishida

Kumamoto University Hospital
Hisao Ogawa
Michio Kawasuji
Seigo Sugiyama
Shoichiro Hagiwara

Kurashiki Central Hospital
Kazuaki Mitsudo
Tatsuhiko Komiya
Kazushige Kadota

Kyoto University Hospital
Takeshi Kimura
Masashi Komeda

Maizuru Kyosai Hospital
Ryozo Tatami
Teruaki Ushijima

Mitsubishi Kyoto Hospital
Akira Yoshida
Hiroyuki Nakajima
Shinji Miki

Nara Hospital, Kinki University School of Medicine
Ryuichi Hattori
Noboru Nishiwaki
Manabu Shirotani

Nishi-Kobe Medical Center
Hiroshi Kato
Hiroshi Eizawa

Osaka Red Cross Hospital
Masaru Tanaka
Kazuaki Minami

Shiga University of Medical Science Hospital
Minoru Horie
Tohru Asai
Hiroyuki Takashima
Ryuji Higashita

Shimabara Hospital
Mamoru Takahashi
Takafumi Tahata
Yoshiki Matoba

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Kiyoshi Doyama
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Appendix B. List of clinical research coordinators

Dear Professor A.J.S. Coats:

Please find our manuscript entitled “Chronic Obstructive Pulmonary Disease—an Independent Risk Factor for Long-term Cardiac and Cardiovascular Mortality in Patients with Ischemic Heart Disease” by Kei Nishiyama et al., which we would like to submit for publication as original research papers. Chronic obstructive pulmonary disease (COPD) and ischemic heart disease (IHD) share smoking as a risk factor, so these two diseases often coexist. Previous studies have shown patients with COPD have a significantly higher risk of long-term all-cause mortality after having PCI and CABG. This study also demonstrated patients with COPD also have higher long-term mortality rates than those without COPD after first elective PCI and CABG. The question of how having COPD affect long-term mortality and morbidity in patients with ischemic heart disease remains unsettled. To our knowledge, this study is the first
report showing patients with COPD have a significantly higher risk of cardiac death and cardiovascular death after having PCI and CABG.

The manuscript has not been published and is not being considered for publication elsewhere in whole or part in any language. All authors have read and approved the manuscript. No conflict of interests exists in any of the authors in this study.

Your kind consideration would be greatly appreciated.

Yours sincerely,

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Kyoto University Graduate School of Medicine,
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Kyoto, 606-8507, Japan
(Tel) 81-7-5751-3198
(Fax) 81-7-5751-3299
(E-mail) keinishi@kuhp.kyoto-u.ac.jp
Table 1. Patient and Disease Characteristics

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<tr>
<td>Age</td>
<td>72.7 ± 7.95</td>
<td>67.2 ± 10.00</td>
</tr>
<tr>
<td>Body mass index</td>
<td>21.7 ± 3.7</td>
<td>23.7 ± 3.2</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention.
Table 3. Cox Proportional-Hazards Model for All-cause Mortality and Cardiac Death

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Not-adjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>All-Cause mortality (n=906)</td>
<td>1.60</td>
<td>1.38-1.83</td>
</tr>
<tr>
<td>Cardiac death (n=376)</td>
<td>1.65</td>
<td>1.31-2.02</td>
</tr>
</tbody>
</table>

HR = hazard ratio; CI = confidential index.
Table 2. In-hospital Outcomes

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>COPD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=240)</td>
<td>No (n=9632)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>3 1.3%</td>
<td>118 1.2%</td>
</tr>
<tr>
<td>In-hospital QMI</td>
<td>2 0.8%</td>
<td>91 0.9%</td>
</tr>
<tr>
<td>MACE</td>
<td>7 2.9%</td>
<td>235 2.4%</td>
</tr>
<tr>
<td>Hospitalization (days)</td>
<td>22.6±29.6</td>
<td>18.1±21.7</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; QMI = Q-wave myocardial infarction; MACE = major adverse cardiac event.