J Chin Med Assoc

ORIGINAL ARTICLE

Impact of medications on outcomes in patients with acute myocardial infarction and chronic obstructive pulmonary disease: A nationwide cohort study

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Abstract

Background: Various inhaled bronchodilators have been associated with cardiovascular safety concerns. This study aimed to investigate the long-term impact of chronic obstructive pulmonary disease (COPD) and the safety of COPD medications in patients after their first acute myocardial infarction (AMI).

Methods: This nationwide cohort study was conducted using data from the Taiwan National Health Insurance Research Database. Patients hospitalized between 2000 and 2012 with a primary diagnosis of first AMI were included and divided into three cohorts (AMI, ST-elevation myocardial infarction [STEMI], and non-STEMI [NSTEMI]). Each cohort was propensity score matched (1:1) with patients without COPD. A Cox proportional hazards regression model was used to estimate hazard ratios (HRs) with 95% CIs.

Results: A total of 186 112 patients with AMI were enrolled, and COPD was diagnosed in 13 065 (7%) patients. Kaplan-Meier curves showed that patients with COPD had a higher mortality risk than those without COPD in all cohorts (AMI, STEMI, and NSTEMI). The HR of mortality in AMI, STEMI, and NSTEMI patients with COPD was 1.12 (95% CI, 1.09-1.14), 1.20 (95% CI, 1.14-1.25), and 1.07 (95% CI, 1.04-1.10), respectively. Short-acting inhaled bronchodilators and corticosteroids increased mortality risk in all three cohorts. However, long-acting inhaled bronchodilators reduced mortality risk in patients with AMI (long-acting beta-agonist [LABA]: HR, 0.87; 95% CI, 0.81-0.94; long-acting muscarinic antagonist [LAMA]: HR, 0.82; 95% CI, 0.69-0.96) and NSTEMI (LABA: HR, 0.89; 95% CI, 0.83-0.97; LAMA: HR, 0.80; 95% CI, 0.68-0.96).

Conclusion: This study demonstrated that AMI patients with COPD had higher mortality rates than those without COPD. Using inhaled short-acting bronchodilators and corticosteroids reduced survival, whereas long-acting bronchodilators provided survival benefits in AMI and NSTEMI patients. Therefore, appropriate COPD medication for acute AMI is crucial.

Keywords: Acute myocardial infarction; Bronchodilators; Chronic obstructive pulmonary disease; Steroids

1. INTRODUCTION

According to the World Health Organization, ischemic heart disease has been the leading cause of death worldwide in recent years. The mortality rate is 8.93 million deaths annually, accounting for nearly 16% of all-cause mortality.[1] Despite the standard medical treatment recommended by American Heart Association/European Society of Cardiology, and the evolution of interventional therapy, acute myocardial infarction (AMI) still causes tremendous morbidity and mortality, thereby burdening the healthcare system.[2] Thus, the factors related to AMI influencing mortality should be addressed.

Chronic obstructive pulmonary disease (COPD), with a prevalence rate of approximately 11.7%, causes serious and long-term disability and early death, accounting for approximately 3.2 million deaths annually.[1] COPD and AMI share common risk factors that promote inflammation, characterized by the enhanced production of chemokines and cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha, which enter the circulation from the lungs. Moreover, inflammation deteriorates preexisting comorbidities and may initiate lung cancer.[3]

Despite the pharmacological management of AMI, systemic inflammation due to COPD promotes atherosclerosis,

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2023) 86: 183-190.

Received April 22, 2022; accepted September 9, 2022.

doi: 10.1097/JCMA.0000000000000835.

endothelial dysfunction, and arterial stiffness;[4] thereby reducing treatment efficacy and survival in patients with AMI. Meanwhile, the main underlying causes of COPD in Asian populations are a high prevalence rate of cigarette smoking and a very high level of air pollution.[5] Whether the different causes of COPD influence the outcome of AMI needs clarification.

Furthermore, the medications for secondary prevention after AMI, such as beta-blockers, have been associated with reduced mortality in patients with COPD.[6] On the other hand, the safety of COPD medications, such as inhaled bronchodilators and corticosteroids, has yet to be investigated in patients with AMI.[7,8] Therefore, this nationwide population-based cohort study aimed to investigate the long-term impact of COPD and the safety of COPD medications in patients with AMI.

2. METHODS

2.1. Data collection

We conducted a nationwide cohort study in Taiwan, including all hospitalized patients with a primary diagnosis of AMI, which was approved by the Human Research Committee of Kaohsiung Veterans General Hospital. Data were retrieved from a full-population dataset from Taiwan's National Health Insurance Research Database (NHIRD). Taiwan launched the National Health Insurance (NHI) program in 1995 and enrolled 99.9% of citizens and legal residents. This dataset contains data for approximately 23 million people whose registration files, diagnosis codes, medications, examinations, and procedures were recorded for reimbursement and research.[9] The accuracy of claimed diagnosis codes have been validated in different studies.[10]

2.2. Study design

We identified all hospitalized patients with a primary diagnosis of AMI (International Classification of Diseases, Ninth Revision [ICD-9], 410-410.92) for the first time between January 2000 and December 2012 in Taiwan. Patients aged <18 years, >120 years, and those with unclear insurance records were excluded. In addition, patients with AMI and a concurrent diagnosis of COPD (ICD-9 codes 491, 492, or 496) were included. Propensity score matching was performed using a 1:1 matching protocol based on sex, age group, comorbidities, and interventions (percutaneous coronary intervention, coronary artery bypass graft, and intra-aortic balloon pump). Patients with AMI were further divided into ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) subtypes. Patients with AMI diagnosed as both STEMI and NSTEMI were excluded. Patients with either subtype in the AMI cohort with a concurrent diagnosis of COPD were identified individually by ICD-9 codes, whereas patients with either subtype in the AMI cohort without COPD were selected by propensity score matching and designated as the control group. We used ICD-9 codes to identify AMI subtypes and comorbidities and anatomical therapeutic chemical codes to analyze the survival influence of COPD and AMI medications during hospitalization.

2.3. Outcome analysis

All enrolled patients were followed up until December 31, 2012, or death, whichever occurred first. The study's primary endpoint was mortality, defined as the end date of NHI coverage. The criteria for mortality are reliable in Taiwan because NHI is mandatorily paid monthly, even in low-income households (the government offers premium subsidies). Thus, the difference between the date of admission and the end date of NHI coverage should be within one month.

2.4. Statistical analyses

Data were analyzed using SAS software (version 9.4; SAS Institute, Inc., Cary, NC). Categorical data are presented as percentages and compared using Chi-square tests. Continuous variables are presented as means and SDs and compared using paired *t*-tests. A Cox proportional hazards model was used to calculate hazard ratios and 95% CIs. Kaplan-Meier analysis was performed to estimate the cumulative survival and differences between patients with AMI and COPD and the control group. A log-rank test was performed to evaluate differences between curves. Differences with a two-tailed p value <0.05 were considered statistically significant.

3. RESULTS

3.1. Descriptive characteristics of the study groups

Between January 2000 and December 2012, 186 326 patients with a primary diagnosis of AMI for the first time were hospitalized. Based on the exclusion criteria, 214 patients were excluded (Fig. 1), and 186 112 patients with AMI were included. Patients with AMI were categorized into STEMI (73 148 patients) and NSTEMI (112 408 patients) cohorts for further analysis. Patients with a concomitant COPD diagnosis were selected. There were 23 704 patients in the overall AMI cohort (6569 in the STEMI cohort and 17 089 in the NSTEMI cohort). Patients without COPD were propensity score matched (1:1) for each cohort (Fig. 1). Patient demographic and clinical characteristics (Table 1) revealed that, in both groups of all cohorts, most patients were male and >65 years of age. No significant differences were observed in comorbidities and coronary vessel interventions between groups, except in the AMI cohort, which had a higher proportion of patients with STEMI and concomitant COPD (32.29% vs. 27.7%; $p <$ 0.0001). In each cohort, patients with COPD were administered more calcium channel blockers, short- and long-acting bronchodilators, Xanthiums, and corticosteroids than those without COPD. In addition, patients without COPD received more antiplatelets, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARB), statins, beta-blockers, and heparin or low-molecular-weight heparin than patients with COPD. No significant differences were observed in the use of vasopressors (dopamine or norepinephrine) and interventions (percutaneous coronary intervention, coronary artery bypass graft, and intra-aortic balloon pump) between the two groups.

3.2. Survival analysis

During the 12-year follow-up, Kaplan-Meier curves suggested that patients with COPD had a higher mortality risk than those without COPD in all cohorts (AMI, STEMI, and NSTEMI). Differences in mortality remained among subgroups for sex, age, hypertension, diabetes mellitus, and percutaneous coronary intervention (log-rank, all $p < 0.0001$; Figs. 2–4). The mortality rates ($p < 0.0001$) were 77.65% and 67.89% in patients with and without COPD in the AMI cohort, respectively; 74.12% and 61.85% in patients with and without COPD in the STEMI cohort, respectively; and 78.99% and 70.52% in patients with and without COPD in the NSTEMI cohort, respectively.

Cox proportional hazards regression analysis revealed that the mortality rate in AMI patients was higher in males, those ≥65 years of age, and those with hypertension, diabetes mellitus, peripheral vascular disease, heart failure, end-stage renal disease, and cerebral vascular accidents (Table 2). COPD in patients with AMI was associated with a 12% higher mortality rate (20% higher in patients with STEMI and 7% higher in patients with NSTEMI). The negative impacts of age and comorbidities on mortality risk were similar in all cohorts (Table 2). Post-AMI medications such as antiplatelets, beta-blockers, ACEI/ARB, and statins substantially reduced mortality risk in all cohorts. However, corticosteroids, short-acting beta-agonists (SABA), and short-acting muscarinic antagonists (SAMA) significantly increased mortality risk in the AMI cohort. The adverse effects

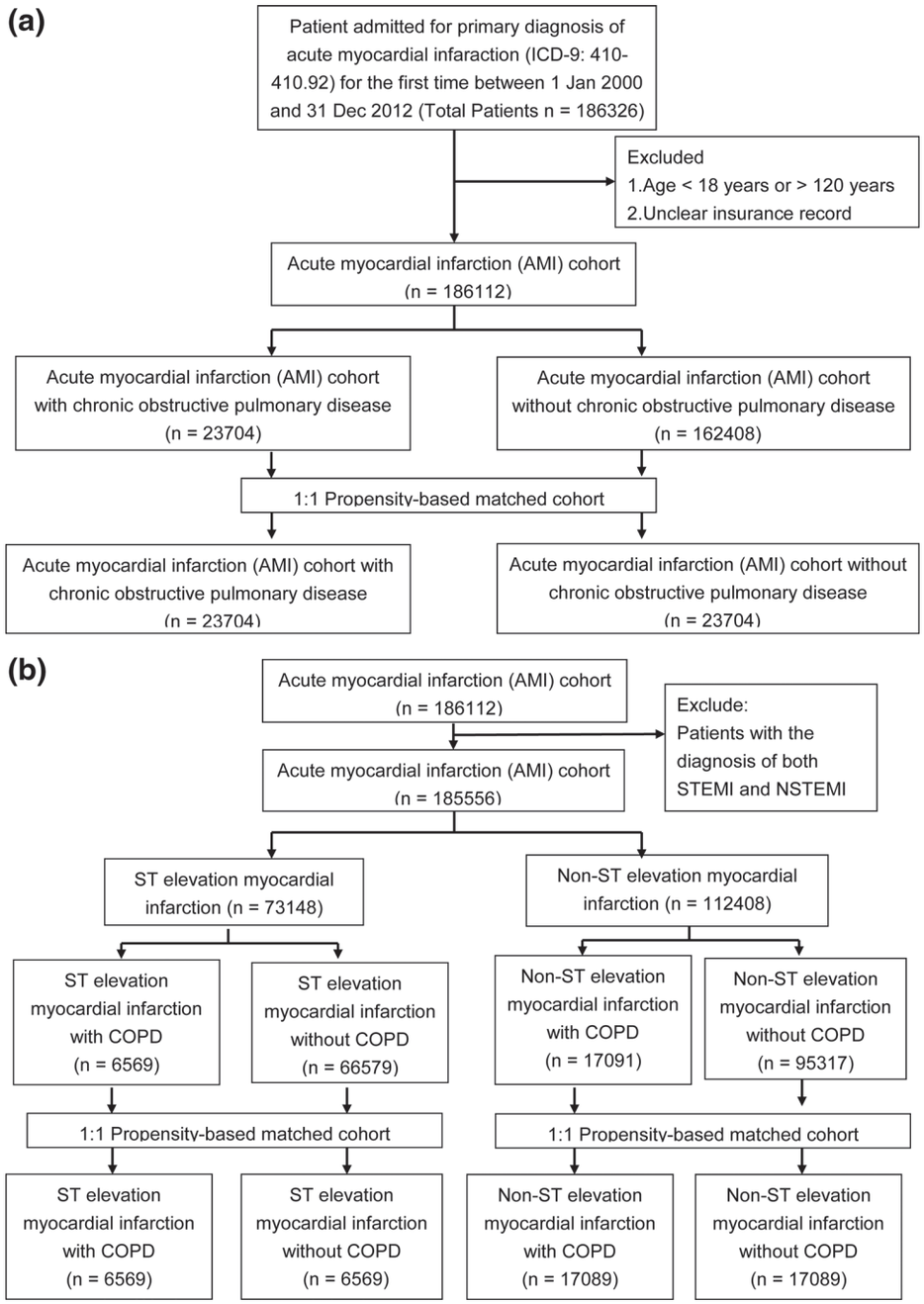

Fig. 1 A, Flow chart for the selection of patients with AMI with and without COPD from the Taiwan National Health Insurance Research Database. B, Flow chart for the selection of STEMI and NSTEMI cohorts with and without COPD from the Taiwan National Health Insurance Research Database. AMI = acute myocardial infarction; COPD = chronic obstructive pulmonary disease; NSTEMI = non-ST-elevation myocardial infarction; STEMI = ST-elevated myocardial infarction.

of corticosteroids and short-acting bronchodilators were consistent in all cohorts. In contrast, long-acting beta-agonists (LABAs), long-acting muscarinic antagonists (LAMA), and Xanthiums significantly increased survival rates in the AMI cohort. Similar results were observed in the NSTEMI cohort; however, no significant survival benefit was observed in the STEMI cohort.

4. DISCUSSION

In this nationwide population-based cohort and propensity score-matched study, AMI, STEMI, and NSTEMI patients with COPD had higher mortality rates than those without COPD. Guidelines suggest that post-AMI medications reduce the mortality rate in all patients with AMI, irrespective of COPD status. However, post-AMI medications are lesser administered to patients with a history of COPD. In contrast, medications for COPD may be misused in patients with AMI without COPD and underused in those with COPD. In patients with AMI, SABA, SAMA, and corticosteroids were associated with a higher mortality rate in all cohorts, whereas LABA, LAMA, and Xanthium were associated with a reduced mortality rate in AMI and NSTEMI cohorts.

Table 1

Demographic and clinical characteristics of AMI, STEMI, and NSTEMI patients with and without COPD

	All AMI			STEMI			NSTEMI		
	With COPD	Without COPD		With COPD	Without COPD		With COPD	Without COPD	
Variables	(n = 23 704)	(n = 23 704)	*p*	(n = 6569)	(n = 6569)	*p*	(n = 17 089)	(n = 17 089)	*p*
Men, n (%)	17524 (73.93)	17514 (73.89)	0.9167	5149 (78.38)	5144 (78.31)	0.9157	12342 (72.22)	12336 (72.19)	0.9422
Age ≥65 y, n (%)	21033 (88.73)	21041 (88.77)	0.9074	5694 (86.68)	5698 (86.74)	0.9181	15299 (89.53)	15308 (89.58)	0.8735
Comorbidities, n (%)									
Hypertension	16810 (70.92)	16813 (70.93)	0.9758	4214 (64.15)	4212 (64.12)	0.971	12564 (73.52)	12559 (73.49)	0.9511
Dyslipidemia	7720 (32.57)	7707 (32.51)	0.8986	2164 (32.94)	2154 (32.79)	0.8527	5542 (32.43)	5522 (32.31)	0.8172
Diabetes mellitus	9334 (39.38)	9373 (39.54)	0.7140	2327 (35.42)	2349 (35.76)	0.6885	6992 (40.92)	7026 (41.11)	0.7085
Peripheral vascular disease	1294 (5.46)	1276 (5.38)	0.7150	272 (4.14)	270 (4.11)	0.9301	1016 (5.95)	1011 (5.92)	0.9088
Heart failure	3783 (15.96)	3782 (15.96)	0.9900	722 (10.99)	715 (10.88)	0.8449	3057 (17.89)	3037 (17.77)	0.7775
End-stage renal disease	839 (3.54)	840 (3.54)	0.9802	145 (2.21)	144 (2.19)	0.9526	693 (4.06)	692 (4.05)	0.9781
Cerebrovascular accident	1000 (4.22)	998 (4.21)	0.9635	253 (3.85)	246 (3.74)	0.7494	746 (4.37)	739 (4.32)	0.8527
STEMI	6568 (27.71)	7654 (32.29)	<0.0001						
Interventions, n (%)									
Percutaneous coronary intervention	7422 (31.31)	7425 (31.32)	0.9763	3130 (47.65)	3123 (47.54)	0.9027	4274 (25.01)	4263 (24.95)	0.8907
Coronary artery bypass graft	1261 (5.32)	1263 (5.33)	0.9674	389 (5.92)	390 (5.94)	0.9705	866 (5.07)	867 (5.07)	0.9803
Intra-aortic balloon pump	1021 (4.31)	1019 (4.30)	0.9639	414 (6.30)	412 (6.27)	0.9427	604 (3.53)	607 (3.55)	0.9301
Medications, n (%)									
Antiplatelet	18437 (77.78)	19202 (81.01)	<0.0001	5609 (85.39)	5789 (88.13)	<0.0001	12790 (74.84)	13375 (78.27)	<0.0001
ACEI or ARB	12463 (52.58)	13331 (56.24)	<0.0001	4112 (62.60)	4248 (64.67)	0.0136	8323 (48.70)	9006 (52.70)	<0.0001
Statin	4830 (20.38)	5586 (23.57)	<0.0001	1479 (22.51)	1650 (25.12)	0.0005	3340 (19.54)	3940 (23.06)	<0.0001
Beta-blocker	7629 (32.18)	10817 (45.63)	<0.0001	2455 (37.37)	3335 (50.77)	<0.0001	5159 (30.19)	7447 (43.58)	<0.0001
Calcium channel blocker	9612 (40.55)	8176 (34.49)	<0.0001	2320 (35.32)	1820 (27.71)	<0.0001	7280 (42.60)	6507 (38.08)	<0.0001
Heparin or LMWH	14210 (59.95)	15408 (65.00)	<0.0001	4711 (71.72)	4983 (75.86)	<0.0001	9466 (55.39)	10348 (60.55)	<0.0001
Dopamine	5070 (21.39)	4998 (21.09)	0.4188	1565 (23.82)	1470 (22.38)	0.0492	3495 (20.45)	3498 (20.47)	0.9679
Norepinephrine	2877 (12.14)	2914 (12.29)	0.2207	657 (10.00)	662 (10.08)	0.8846	2165 (12.67)	2324 (13.60)	0.0109
Spironolactone	3374 (14.23)	2994 (12.63)	<0.0001	840 (12.79)	707 (10.76)	0.0003	2529 (14.80)	2311 (13.52)	0.0007
Long-acting muscarinic antagonist	31 (0.47)	4 (0.06)	<0.0001	31 (0.47)	4 (0.06)	<0.0001	189 (1.11)	12 (0.07)	<0.0001
Long-acting beta-agonist	221 (3.36)	32 (0.49)	<0.0001	221 (3.36)	32 (0.49)	<0.0001	886 (5.18)	128 (0.75)	<0.0001
Xanthium	2371 (36.09)	642 (9.77)	<0.0001	2371 (36.09)	642 (9.77)	<0.0001	6172 (36.12)	1925 (11.26)	<0.0001
Corticosteroid	1504 (22.90)	566 (8.62)	<0.0001	1504 (22.90)	566 (8.62)	<0.0001	5884 (34.43)	2890 (16.91)	<0.0001
Short-acting muscarinic antagonist	3050 (46.43)	1386 (21.10)	<0.0001	3050 (46.43)	1386 (21.10)	<0.0001	9380 (54.89)	5114 (29.93)	<0.0001
Short-acting beta-agonist	2384 (36.29)	1067 (16.24)	<0.0001	2384 (36.29)	1067 (16.24)	<0.0001	6525 (38.18)	3527 (20.64)	<0.0001

ACEI = angiotensin-converting enzyme inhibitor; AMI = acute myocardial infarction; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; LMWH = low-molecular-weight heparin; NSTEMI = non-ST-elevated myocardial infarction; STEMI = ST-elevated myocardial infarction.

AMI is associated with higher inhospital, short-term, and long-term mortality.[11] The largest retrospective study conducted in the UK showed that both inhospital and 180-day mortality increased in patients with AMI and COPD.[12] A systematic review and meta-analysis, including observational studies from Europe and the US, demonstrated that mortality risk is 26% higher in patients with AMI and COPD than in those with AMI without COPD.[13] However, the heterogeneity of the meta-analysis was high (I^2 = 74%), the number of patients included was <10 000, and the follow-up duration was variable (1-7 years). Our study used data from a nationwide, full-population database that provided long-term follow-up data. Our study suggests that COPD is an independent risk factor for long-term mortality in patients with AMI. This result was also observed in the STEMI and NSTEMI cohorts.

An analysis using the largest nationwide AMI registry in the US showed that STEMI was associated with higher mortality within 90 days than NSTEMI, but the difference was reduced after multivariant adjustment after 90 days.[14] Our study demonstrated that patients with STEMI had lower long-term mortality than those with NSTEMI. This may be because patients with STEMI received more medications for secondary prevention and had a higher incidence of coronary artery interventions than those with NSTEMI (Table 1). STEMI has been associated with early mortality; however, our findings suggest that patients with NSTEMI require more aggressive evidence-based management than those with STEMI.

In the West, patients with AMI and COPD have received fewer evidence-based AMI medications.[13–15] Our study revealed a similar trend of medication underusage, which is common in Taiwan. It is not surprising that the beta-blocker prescription rate is lower in patients with AMI and COPD. The use of beta-blockers in COPD raises concerns regarding acute exacerbation despite recent studies proving its safety.[16] Underusing standard postmyocardial infarction medications has been shown to cause inferior outcomes.[13,17]

The present study showed that SABA and SAMA were associated with 30% and 20% higher mortality rates, respectively (Table 2). Intriguingly, no adverse effect on survival was observed using long-acting bronchodilators. A previous systematic review and meta-analysis investigating the association between inhaled bronchodilators and AMI revealed that tiotropium had a protective effect against myocardial infarction (26% risk reduction). Still, short-acting beta-2 agonists slightly increased the risk of myocardial infarction after the first inhalation.[18] The differences in mortality rate due to short- and long-acting inhaled bronchodilators may be due to long-acting bronchodilators relieving airway obstruction and deflating the lungs. Hyperinflation of the lungs increases intrathoracic pressure and subsequently decreases the preload of the right

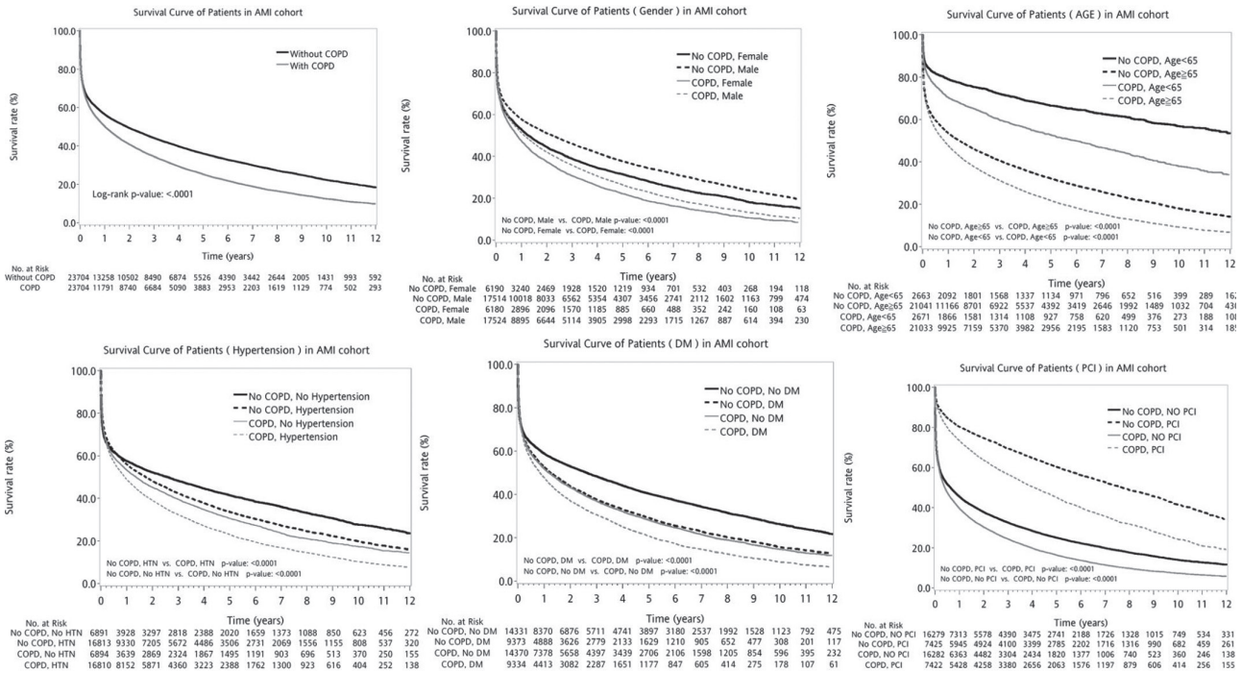

Fig. 2 Kaplan-Meier survival curve for AMI comparing patients with and without COPD and in different subgroups, including sex, age, hypertension, diabetes mellitus, and percutaneous coronary intervention. AMI = acute myocardial infarction; COPD = chronic obstructive pulmonary disease.

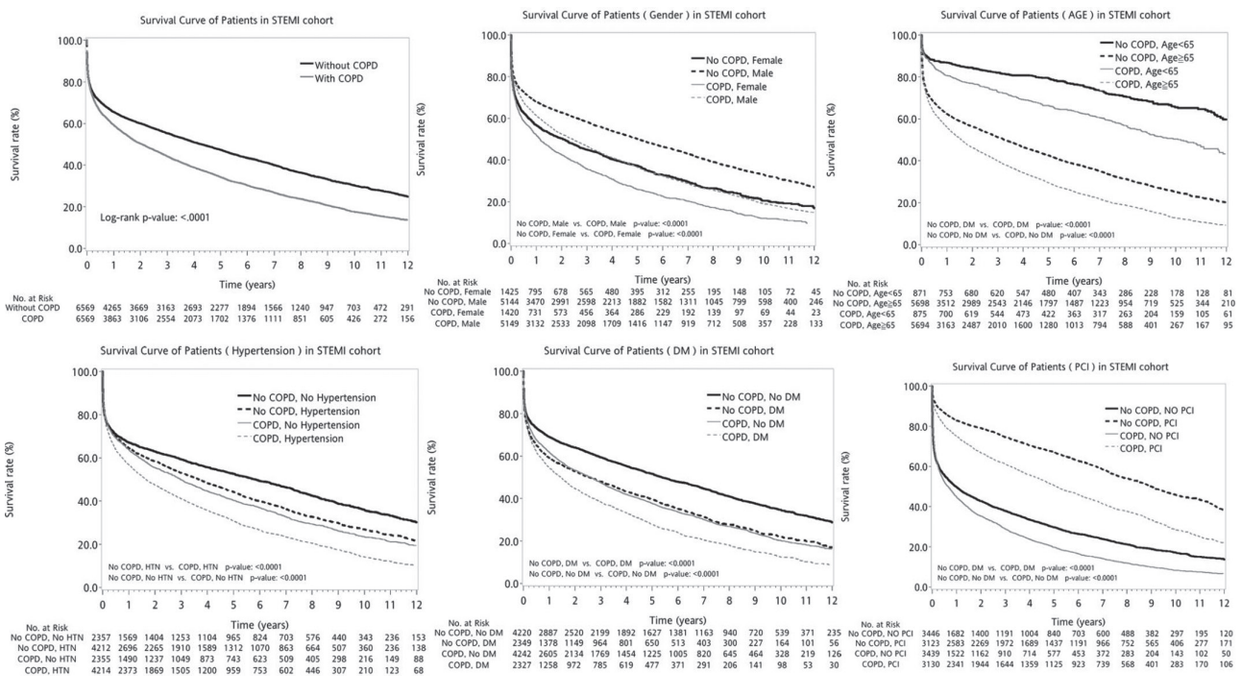

Fig. 3 Kaplan-Meier survival curve for STEMI comparing patients with and without COPD and in different subgroups including sex, age, hypertension, diabetes mellitus, and percutaneous coronary intervention. COPD = chronic obstructive pulmonary disease; STEMI = ST-elevation myocardial infarction.

ventricle. In addition, pulmonary vessels are also compressed by alveolar overdistension.[19] An observational study demonstrated that COPD compromised the circulatory system to compensate for the hemodynamic changes during AMI.[20] Inhalation of long-acting bronchodilators has been shown to increase the stroke volume and cardiac index by 10% in both left and right ventricles without altering heart rate and blood pressure.[21,22] We hypothesized that long-acting bronchodilators contributed to sustained lung deflation for over 24 hours, thereby reducing the cardiac load and oxygen demand, which might provide protective effects after an AMI event. In contrast, short-acting bronchodilators have a shorter half-life, making it difficult to achieve a similar magnitude of bronchodilation and lung deflation for over 24 hours.

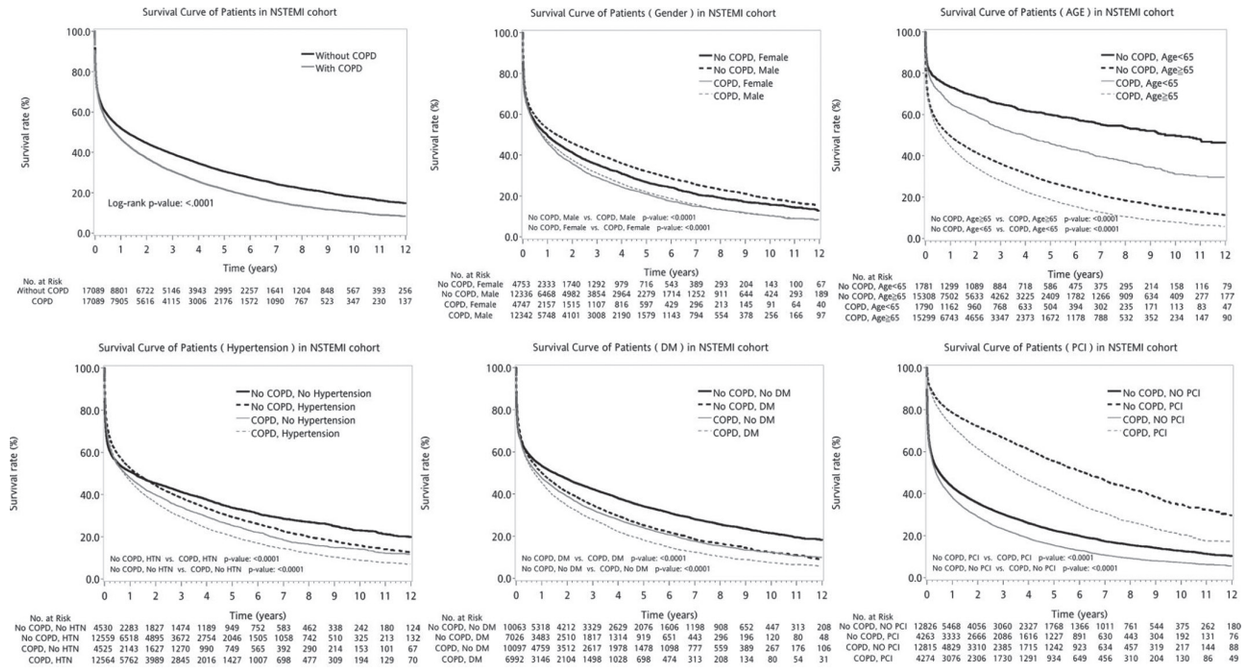

Fig. 4 Kaplan-Meier survival curve for NSTEMI comparing patients with and without COPD and in different subgroups, including sex, age, hypertension, diabetes mellitus, and percutaneous coronary intervention. COPD = chronic obstructive pulmonary disease; NSTEMI = non-ST-elevation myocardial infarction.

Table 2

Cox proportional hazards regression analysis in patients with AMI with and without COPD

	All AMI (n = 23 704)		STEMI (n = 6569)		NSTEMI(n = 17 089)	
Variables	**Adjusted HR (95% CI)**	***p***	**Adjusted HR (95% CI)**	***p***	**Adjusted HR (95% CI)**	***p***
Male	1.09 (1.06-1.12)	<0.0001	0.97 (0.92-1.01)	0.1587	1.10 (1.07-1.13)	<0.0001
Age≥65y	2.24 (2.15-2.34)	<0.0001	2.45 (2.25-2.66)	<0.0001	2.10 (2.00-2.20)	<0.0001
Comorbidities						
COPD	1.12 (1.09-1.14)	<0.*0001*	1.20 (1.15-1.26)	<0.*0001*	1.07 (1.04-1.10)	<0.*0001*
Hypertension	1.09 (1.07-1.12)	<0.0001	1.15 (1.10-1.20)	<0.0001	1.08 (1.05-1.11)	<0.0001
Diabetes mellitus	1.25 (1.22-1.28)	<0.0001	1.31 (1.25-1.37)	<0.0001	1.22 (1.18-1.25)	<0.0001
Peripheral vascular disease	1.36 (1.30-1.42)	<0.0001	1.37 (1.24-1.51)	<0.0001	1.32 (1.25-1.38)	<0.0001
Heart failure	1.27 (1.23-1.30)	<0.0001	1.37 (1.29-1.46)	<0.0001	1.26 (1.22-1.30)	<0.0001
End-stage renal disease	1.61 (1.52-1.70)	<0.0001	1.60 (1.40-1.81)	<0.0001	1.54 (1.45-1.64)	<0.0001
Cerebral vascular accident	1.06 (1.01-1.12)	0.0227	1.16 (1.05-1.29)	0.0049	1.08 (1.02-1.14)	0.0129
STEMI	0.91 (0.89-0.94)	<0.0001				
Interventions						
Percutaneous coronary intervention	0.50 (0.49-0.51)	<0.0001	0.49 (0.47-0.52)	<0.0001	0.50 (0.49-0.52)	<0.0001
Coronary artery bypass graft	0.51 (0.49-0.54)	<0.0001	0.53 (0.48-0.58)	<0.0001	0.50 (0.47-0.57)	<0.0001
Intra-aortic balloon pump	1.99 (1.88-2.10)	<0.0001	2.04 (1.87-2.23)	<0.0001	1.85 (1.72-1.98)	<0.0001
Medications						
Antiplatelet	0.75 (0.73-0.77)	<0.0001	0.89 (0.84-0.95)	0.0003	0.71 (0.68-0.73)	<0.0001
ACEI or ARB	0.76 (0.47-0.78)	<0.0001	0.77 (0.74-0.81)	<0.0001	0.74 (0.72-0.77)	<0.0001
Statin	0.85 (0.81-0.88)	<0.0001	0.83 (0.76-0.90)	<0.0001	0.85 (0.81-0.90)	<0.0001
Beta-blocker	0.86 (0.84-0.88)	<0.0001	0.90 (0.86-0.94)	<0.0001	0.85 (0.83-0.88)	<0.0001
Long-acting muscarinic antagonist	0.82 (0.69-0.96)	0.0162	0.75 (0.46-1.21)	0.2342	0.80 (0.68-0.96)	0.0143
Long-acting beta-agonist	0.87 (0.81-0.94)	0.0001	0.91 (0.77-1.07)	0.2458	0.89 (0.83-0.97)	0.0044
Xanthium	0.94 (0.91-0.96)	<0.0001	0.94 (0.89-1.00)	0.0336	0.93 (0.90-0.96)	<0.0001
Corticosteroid	1.10 (1.07-1.14)	<0.0001	1.09 (1.02-1.16)	0.0104	1.12 (1.09-1.16)	<0.0001
Short-acting antimuscarinic agent	1.30 (1.26-1.34)	<0.0001	1.42 (1.33-1.52)	<0.0001	1.25 (1.20-1.30)	<0.0001
Short-acting beta-agonist	1.20 (1.16-1.23)	<0.0001	1.17 (1.09-1.24)	<0.0001	1.20 (1.16-1.25)	<0.0001

ACEI = angiotensin-converting enzyme inhibitor; AMI = acute myocardial infarction; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; HR, hazard ratio; NSTEMI = non-ST-elevated myocardial infarction; STEMI = ST-elevated myocardial infarction.

This study also showed that approximately one to six patients with AMI without a history of COPD were prescribed SABA and SAMA (Table 1). This may be due to acute pulmonary edema resembling obstructive lung disease symptoms.[23] On the other

hand, <5% of patients with COPD had continued using either LABA or LAMA during AMI, while nearly half of the patients with COPD used short-acting bronchodilators (Table 1). Prescription of short-acting bronchodilators under the conditions mentioned above led to higher mortality rates in patients with AMI. Higher mortality rates with short-acting bronchodilators have also been observed in patients with AMI and COPD. Furthermore, LABA is often used in combination with inhaled corticosteroids. Sudden withdrawal of LABA during hospitalization and interruption of inhaled corticosteroids increases the risk of acute exacerbation of COPD in patients with a history of exacerbation or high eosinophil counts.[24] Therefore, it is suggested that a standard post-AMI pharmacological checklist should include long-acting bronchodilators.

Corticosteroids have anti-inflammatory effects and have been recommended in chronic obstructive lung disease guidelines for patients with group D COPD and COPD with a high eosinophil count. Steroids reduce the restenosis rate of bare metal stents.[25] In patients with high C-reactive protein levels, oral prednisolone reduced restenosis (relative risk: 0.18) and the risk of major cardiovascular adverse events.[26] However, the detrimental effects of corticosteroids in patients with AMI include impaired wound healing and thinning of the myocardial wall, leading to ventricular wall rupture.[27] A meta-analysis of corticosteroid treatment in patients with AMI revealed a 26% reduction in mortality[28]; however, the mortality benefit was not evident when the analysis was restricted to randomized trials and larger studies. Notably, no conclusive harm was associated with corticosteroids in the meta-analysis. In contrast, our findings suggest that corticosteroid use is associated with a higher mortality rate, even in patients with COPD, with the STEMI and NSTEMI cohorts showing similar risks. The post-AMI care plan should consider weighing the benefits and risks of corticosteroids in patients with AMI and COPD.

Our study has several strengths. First, we analyzed a full-population dataset, which included data from 23 million Taiwanese residents. There was no selection bias resulting from the sampling. Second, the results obtained from the NHIRD dataset can be generalized to the entire population. Third, in our study, patients >65 years old compromised nearly 90% of those enrolled. Generally, elderly individuals are rarely enrolled in randomized clinical trials.[29] Our study analyzed long-term follow-up data to identify the risk factors for mortality due to AMI and the effectiveness of medications.

On the other hand, our study also has several limitations. First, although we used propensity score matching to balance baseline characteristics between groups, unmeasurable confounding factors could have existed. Second, because the NHIRD database did not contain information about body mass index, smoking habits, and severity of COPD, we could not analyze their effects. Third, the diagnosis of AMI and COPD was based on the ICD-9. However, the accuracy of the main diagnosis in the NHIRD, including AMI and COPD, has been individually validated.[30,31] Fourth, we could not evaluate adherence to evidence-based post-AMI medications during the follow-up period.

In conclusion, patients with AMI and COPD have higher mortality rates than those without COPD. The STEMI and NSTEMI cohorts showed consistent results. Short-acting bronchodilators and corticosteroids are associated with increased mortality during AMI. Long-acting bronchodilators are associated with reduced mortality risk; however, they are rarely prescribed for AMI. Our study emphasizes that COPD medications also affect AMI outcomes. Therefore, multidisciplinary care, incorporated with a pulmonologist to evaluate appropriate COPD medications after AMI, is crucial for improving survival.

ACKNOWLEDGMENTS

The authors would like to thank Yong-Chih Chiu, Hsiao-Chin Lin, Tzu-Jung Chuang, Hsiao-Ching Kuo, and Chia-Jung Chin for their assistance with statistical analyses.

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