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Risk of Cardiovascular Events Associated with Chronic Obstructive Pulmonary Disease and/or Metabolic Syndrome: A Large-Scale Nationwide Population-Based Cohort Study

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Purpose: Chronic obstructive pulmonary disease (COPD) and metabolic syndrome (MetS) are among the most prevalent conditions that might predispose individuals to life-threatening events. We aimed to examine their associations with cardiovascular (CV) events and mortality using a large-scale population dataset from the National Health Information Database in Korea.

Patients and Methods: This population-based cohort study enrolled adults aged ≥40 years who had undergone more than two health examinations between 2009 and 2011. They were divided into four groups based on the presence of COPD and MetS. Analysis of the outcomes and CV events or deaths was performed from 2014 to 2019. We compared CV event incidence and mortality rates using a multivariate Cox proportional hazards model and Kaplan–Meier curves.

Results: Totally, 5,101,810 individuals were included, among whom 3,738,458 (73.3%) had neither COPD nor MetS, 1,193,014 (23.4%) had only MetS, 125,976 (2.5%) had only COPD, and 44,362 (0.9%) had both. The risk of CV events was significantly higher in individuals with both COPD and MetS than in those with either COPD or MetS alone (HRs: 2.4 vs 1.6 and 1.8, respectively; all P <0.001). Similarly, among those with both COPD and MetS, all-cause and CV mortality risks were also elevated (HRs, 2.9 and 3.0, respectively) compared to the risks in those with either COPD (HRs, 2.6 and 2.1, respectively) or MetS (HRs, 1.7 and 2.1, respectively; all P <0.001).

Conclusion: The comorbidity of MetS in patients with COPD increases the incidence of CV events and all-cause and cardiovascular mortality rates.

Keywords: cardiovascular event, chronic obstructive pulmonary disease, metabolic syndrome

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation, and cardiovascular (CV) events (such as myocardial infarction and stroke) are its most common comorbidities. The systemic inflammatory response caused by COPD may increase the risk of CV events.[1–4] Patients with COPD exhibit elevated CV event risk, with such events contributing significantly to their mortality rate and accounting for one-fourth of deaths.[5] Metabolic syndrome (MetS) is characterized by abdominal obesity, high blood pressure, insulin resistance, impaired glucose metabolism, and dyslipidemia. A chronic low-grade inflammatory state and oxidative stress are responsible for the development of CV events in patients with MetS.[6] MetS is also significantly associated with the incidence of CV events and cardiovascular and all-cause mortality.[7]

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COPD and MetS are linked to systemic inflammatory responses and physical inactivity.[8,9] The evidence strongly suggests that oxidative stress and systemic inflammation play significant roles in the development of COPD and related conditions, such as MetS.[10,11] In individuals with COPD, lung inflammation leads to increased levels of inflammatory markers and cytokines in the systemic circulation.[12] This contributes to ongoing low-grade inflammation and may potentially lead to cardiovascular comorbidities.[13] In patients with COPD, coexisting MetS was independently associated with a greater predicted forced expiratory volume in 1 second (FEV1) and higher rates of heart failure and coronary artery disease.[14] However, there is no research on the impact of coexisting COPD and MetS on CV event incidence or mortality in a large general population cohort.

We aimed to examine the effects of COPD and MetS on the incidence and mortality of CV events using a large-scale population dataset from the National Health Information Database (NHID) established by the Korean National Health Insurance Service.

Materials and Methods

Data Source and Study Population

We enrolled adults aged ≥40 years in this retrospective population-based cohort study. We used data from the NHID, which monitors the health status of almost the entire Korean population. The data comprised anthropometric details (age, sex, height, weight, and body mass index [BMI]), diagnostic information in the form of the International Classification of Disease, tenth revision (ICD-10) codes, laboratory data (such as triglyceride [TG], high- and low-density lipoprotein cholesterol [HDL-C and LDL-C, respectively], and total cholesterol concentrations), systolic and diastolic blood pressure (SBP and DBP, respectively), and social history data including smoking status and weekly alcohol consumption frequency.

Initially, we included participants aged ≥40 years from at least two national health screening programs between 2009 and 2011. Thereafter, we excluded individuals diagnosed with myocardial infarction (I21, I22, I23) or ischemic stroke (I63, I64) between 2002 and 2011 and those who had died by 2011 and had unidentifiable data for COPD or MetS according to the dataset provided by the National Statistics Office. The total number of eligible participants was 5,101,810 (Figure 1).

The study design is depicted in Figure 1. Participants were enrolled between 2009 and 2011, followed by a 2-year washout period (2012–2013), with outcomes evaluated from 2014 to 2019. The washout period aimed to mitigate any residual effects from the pre-enrollment period, and participants with CV events in the two years following enrollment were excluded to minimize "reverse causality" influence. The enrolment period was from 2009 to 2011, followed by a two-year wash-out period from 2012 to 2013. We excluded CV events that developed within two years after the enrolment period to minimize the effect of the exposure before the follow-up period on the primary outcome. Analysis of the outcomes of interest was performed for 2014−2019.

The study protocol was approved by the Institutional Review Board (No. CR320340), and the principles of the Declaration of Helsinki were adhered to. Anonymous and de-identified information was used in our study, and the requirement for informed consent was waived.

Definitions of COPD and MetS

The COPD cohort included patients aged ≥40 years who were assigned an ICD-10 code of COPD (J42, J43, and J44) with a primary or secondary diagnosis and a prescription of at least one of the following medications: inhaled corticosteroids (ICSs), inhaled long-acting β2-agonists (LABAs), an ICS and a LABA combined in a single inhaler (ICS/LABA), inhaled short-acting β2-agonists (SABAs), inhaled long-acting muscarinic antagonists (LAMAs), short-acting muscarinic antagonists (SAMAs), a SAMA and a SABA combined in a single inhaler (SAMA/SABA), oral leukotriene antagonists, xanthine derivatives, mast cell stabilizers, and systemic corticosteroids.[15]

Individuals with three or more of the following components were considered to have MetS: (i) abdominal obesity (waist circumference of ≥90 cm for males or ≥85 cm for females according to the Korean Society for the Study of Obesity Guidelines);[16] (ii) hypertriglyceridemia (serum TG concentration of ≥150 mg/dL or receiving a specific

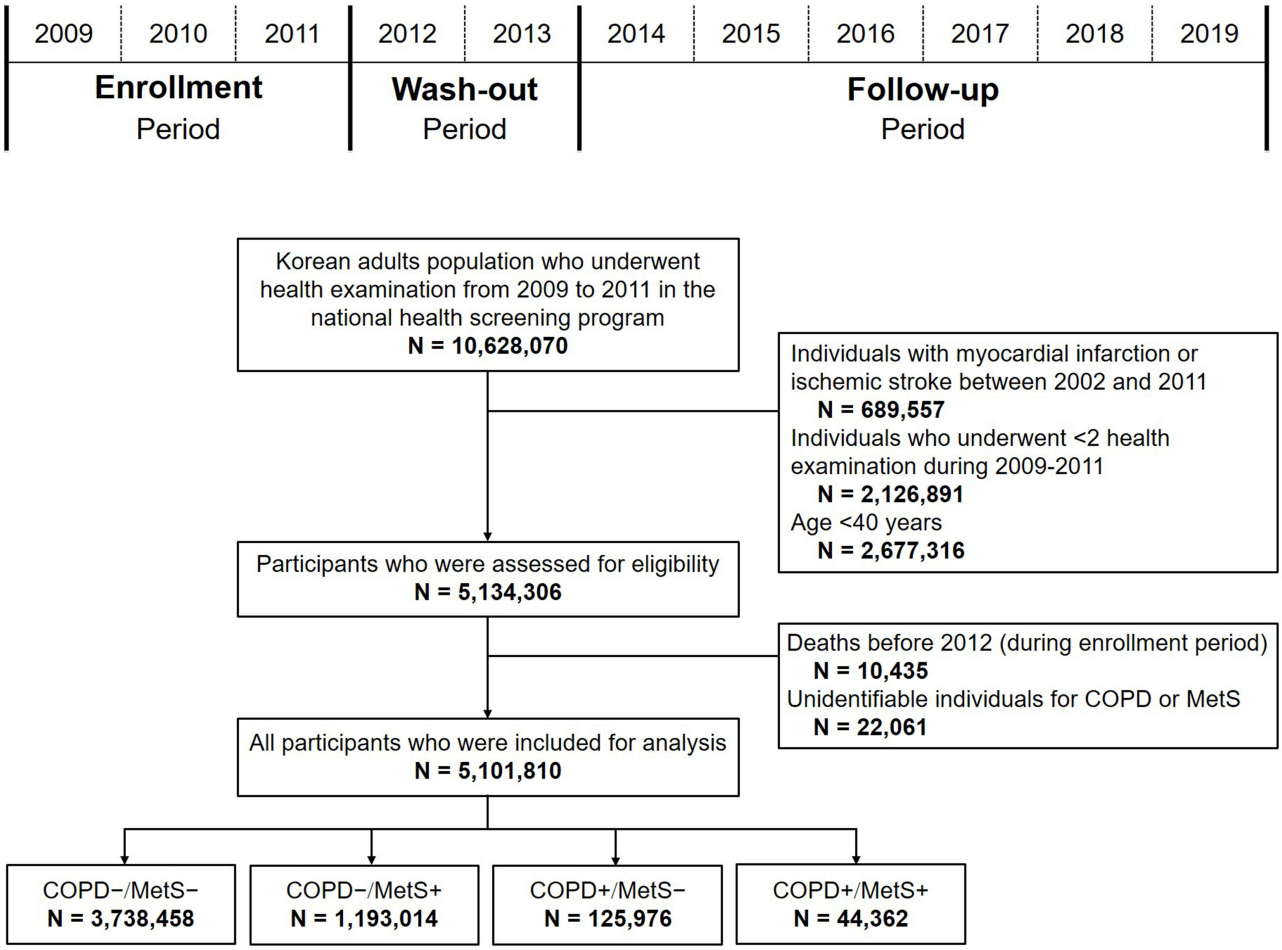


Figure 1 Study design, criteria for inclusion and exclusion, and groups of participants.
Abbreviations: COPD, chronic obstructive pulmonary disease; MetS, metabolic syndrome; +, disease exists; –, disease does not exist.

treatment); (iii) a low serum HDL-C concentration (<40 mg/dL for males or <50 mg/dL for females or receiving a specific treatment); (iv) high blood pressure (SBP ≥ 130 mmHg and DBP ≥ 85 mmHg or treatment with antihypertensive agents); and (v) a high fasting blood glucose level (≥100 mg/dL or treatment with antidiabetic medication).[17]

Definitions of the Outcomes of Interest

The primary outcome of interest was an incident CV event. This was defined as a primary diagnosis such as ischemic heart disease (I20–I25) or stroke (I60–I64) diagnosed ≥2 times or involving hospitalization for ≥4 during the follow-up.

Outcomes related to mortality (all-cause and CV mortality) were defined as a recording of a death code within the NHID database and a CV cause of death (I00-I99).

Data Analyses

Descriptive statistics were used to analyze the baseline characteristics. Categorical variables are presented as frequencies (%), and continuous variables are described as the mean (± standard deviation [SD]). The categorical variables were compared using the chi-squared test, while continuous variables were compared using one-way analysis of variance. We compared the participants based on the presence of COPD and MetS. Participants were followed up from January 1, 2009, until the date of the CV event, death, or December 31, 2019. All outcomes were analyzed using Cox proportional hazards regression analysis while controlling for baseline covariates. Incidence curves were constructed using the Kaplan–Meier method. Statistical significance was set at a two-tailed p-value less than 0.05. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA) and R version 3.4.1 (The R Foundation for Statistical Computing).

Results

Study Population

The participants were divided into four groups based on the presence of COPD and MetS (Table 1). The groups differed in terms of sex; the COPD-/MetS- group had the highest proportion of females, and the COPD-/MetS+ had the lowest (50.4% vs 40.0%). In terms of age distribution, the COPD- groups had more participants aged 40–59 years, and the COPD+ group had more participants aged 60–89 years. Table 1 presents the demographic variables and risk factors for the four groups.

Table 1 Demographic Data of Study Participants

Variable	COPD				P-value
	Yes *N* = 170,338		No *N* = 4,931,472		
	Metabolic Syndrome				
	Yes *N* = 44,362	No *N* = 125,976	Yes *N* = 1,193,014	No *N* = 3,738,458	
Female (%)	21,992(49.6)	58,122(46.1)	477,355(40.0)	1,882,871(50.4)	< 0.0001
Age, years (%)					< 0.0001
40–49	5,285(11.9)	22,176(17.6)	407,777(34.2)	1,658,067(44.4)	
50–59	11,762(26.5)	34,390(27.3)	405,922(34.0)	1,205,019(32.2)	
60–69	16,168(36.5)	40,506(32.2)	269,563(22.6)	636,716(17.0)	
70–79	10,034(22.6)	25,651(20.4)	101,309(8.5)	219,000(5.9)	
80–89	1092(2.5)	3184(2.5)	8268(0.7)	19,113(0.5)	
>90	21(0.1)	69(0.1)	175(0.0)	543(0.0)	
Height, cm	160.4±9.2	160.6±8.6	163.3±9.2	161.9±8.6	< 0.0001
Weight, kg	66.6±10.6	59.6±9.3	69.5±11.1	61.3±9.5	< 0.0001
BMI, kg/m^2	25.8±3.1	23.1±2.9	26.0±4.1	23.3±2.9	< 0.0001
Smoking status					< 0.0001
Never (%)	27,738(63.0)	77,787(62.1)	658,472(55.6)	2,396,550(64.6)	
Former (%)	7285(16.5)	21,267(17.0)	223,586(18.9)	583,522(15.7)	
Current (%)	9038(20.5)	26,127(20.9)	303,230(25.6)	732,823(19.7)	
Alcohol status (per week, %)					< 0.0001
Never	23,847(64.7)	80,452(64.7)	606,522(51.5)	2,082,101(56.5)	
1	5301(12.1)	16,761(13.5)	202,640(17.2)	703,094(19.1)	
2	3756(8.6)	10,174(8.2)	159,121(13.5)	422,284(11.5)	
3	2740(6.3)	7003(5.6)	107,457(9.1)	249,543(6.8)	
4	1034(2.4)	2493(2.0)	36,596(3.1)	80,931(2.2)	
5	841(1.9)	2135(1.7)	26,787(2.3)	58,489(1.6)	
6	576(1.3)	1589(1.3)	14,428(1.2)	32,270(0.9)	
7	1189(2.7)	3674(3.0)	24,517(2.1)	58,584(1.6)	

(*Continued*)

Table 1 (Continued).

Variable	COPD				P-value
	Yes *N* = 170,338		No *N* = 4,931,472		
	Metabolic Syndrome				
	Yes *N* = 44,362	No *N* = 125,976	Yes *N* = 1,193,014	No *N* = 3,738,458	
MetS components					
Waist circumference, cm	88.0±8.8	80.1±8.4	87.3±9.0	79.0±8.2	< 0.0001
TG, mg/dL	194.7±111.0	116.0±69.1	207.2±122.5	117.2±73.6	< 0.0001
Total cholesterol, mg/dL	204.5±48.0	194.4±40.0	206.0±122.5	197.7±39.7	< 0.0001
HDL-C, mg/dL	50.0±34.0	58.9±39.3	49.2±31.6	58.5±34.7	< 0.0001
LDL-C, mg/dL	120.0±83.0	119.3±81.4	119.7±91.8	120.2±86.6	0.4788
SBP, mmHg	131.7±15.8	123.1±14.7	131.3±15.5	121.2±14.2	< 0.0001
DBP, mmHg	81.3±10.3	75.8±9.4	82.1±10.4	75.5±9.5	< 0.0001
Fasting serum glucose, mg/dL	109.9±30.6	95.9±19.5	110.9±32.3	95.4±19.7	< 0.0001

Abbreviations: COPD, chronic obstructive pulmonary disease; BMI, body mass index; MetS, metabolic syndrome; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; SD, standard deviation.

Risk of Cardiovascular Events

The frequency of incident CV events was the lowest (11.7%) for the COPD-/MetS- group and highest (28.6%) for the COPD+/MetS+ group (Table 2). The proportion of newly diagnosed participants with CV events was higher for those with only COPD (21.9%) than for those with only MetS (18.5%). Cardiovascular events in COPD were analyzed

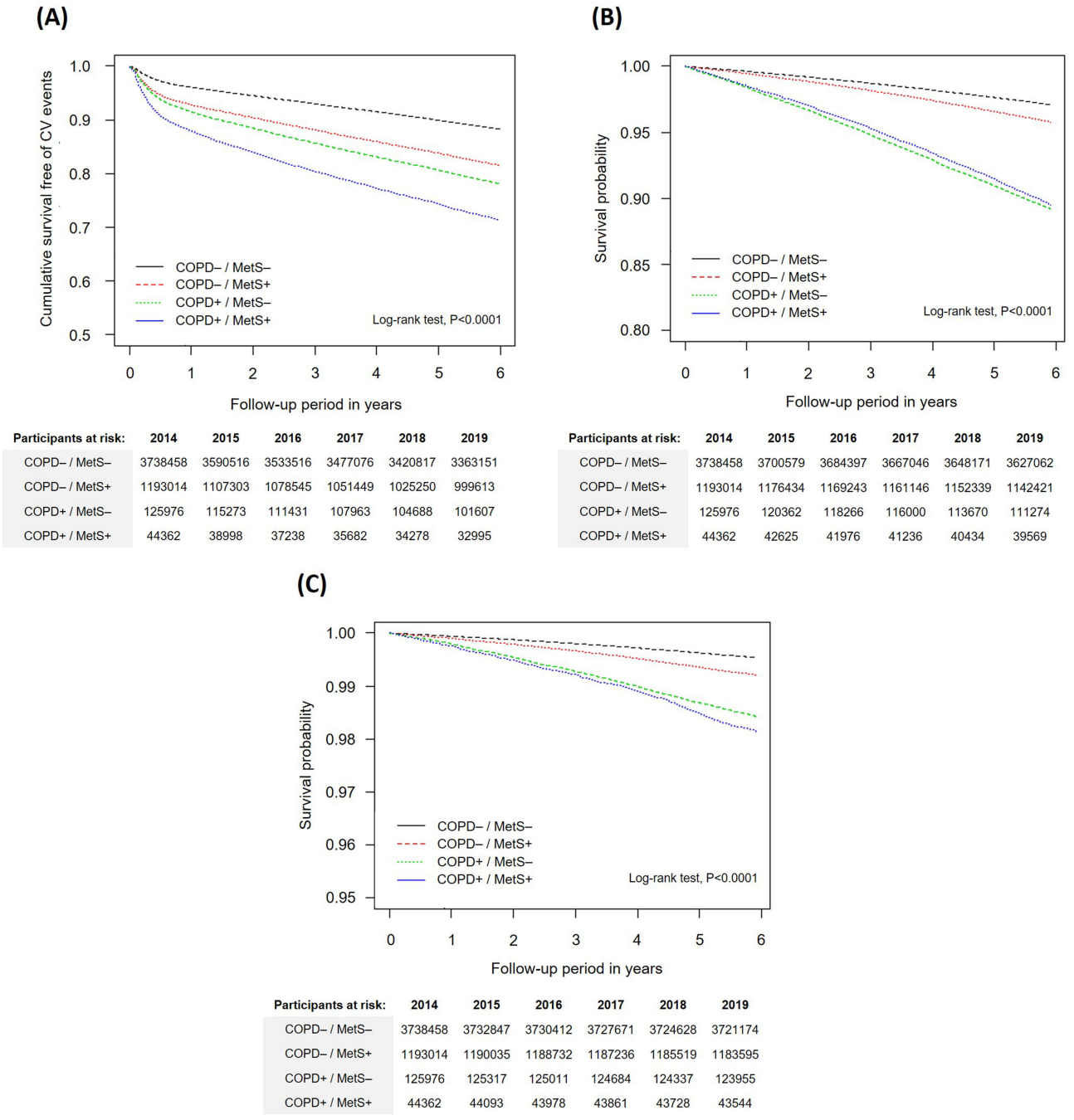
Table 2 Incidence and Hazard Ratios of Cardiovascular Events, All-Cause Mortality, and Cardiovascular Mortality Adjusted for Age, Sex, Smoking Status, and Alcohol Consumption for Participants Grouped by the Presence of COPD and MetS

Variable	No. (%)	Incidence Rate/1000 Person-Years	Hazard Ratio (95% CI)			P-value
			Crude	Model 1†	Model 2‡	
Cardiovascular event						
COPD–/MetS–	438,477(11.7)	11.1	1	1	1	< 0.001
COPD–/MetS+	220,682(18.5)	20.4	2.032(2.484–2.545)	1.775(1.765–1.784)	1.770(1.760–1.779)	
COPD+/MetS–	27,593(21.9)	24.9	2.514(2.021–2.043)	1.662(1.642–1.683)	1.645(1.625–1.666)	
COPD+/MetS+	12,698(28.6)	35.4	3.777(3.711–3.845)	2.386(2.344–2.429)	2.368(2.326–2.411)	
All-cause mortality						
COPD–/MetS–	158,219(4.2)	3.9	1	1	1	< 0.001
COPD–/MetS+	72,471(6.1)	6.4	2.120(2.101–2.140)	1.756(1.740–1.772)	1.743(1.727–1.759)	
COPD+/MetS–	19,490(15.5)	17.0	5.482(5.400–5.565)	2.633(2.594–2.674)	2.557(2.518–2.597)	
COPD+/MetS+	6620(14.9)	17.0	6.254(6.101–6.410)	3.004(2.930–3.079)	2.932(2.860–3.007)	
Cardiovascular mortality						
COPD–/MetS–	25,212(0.7)	1.2	1	1	1	< 0.001
COPD–/MetS+	13,606(1.1)	1.4	2.567(2.512–2.624)	2.067(2.023–2.112)	2.058(2.014–2.104)	
COPD+/MetS–	2773(2.2)	1.5	5.012(4.818–5.214)	2.215(2.128–2.306)	2.144(2.059–2.232)	
COPD+/MetS+	1161(2.6)	1.5	7.146(6.734–7.582)	3.050(2.874–3.237)	2.968(2.795–3.152)	

Notes: †Model 1: additionally adjusted for age and sex. ‡Model 2: model 1 + additionally adjusted for smoking status and alcohol consumption.
Abbreviations: COPD, chronic obstructive pulmonary disease; MetS, metabolic syndrome; CV, cardiovascular; No, number of events; +, disease exists; –, disease does not exist.

according to the number of metabolic syndrome components present. The hazard ratio (HR) for the presence of one component was 1.271 (95% confidence interval [CI]: 1.260–1.283), the HR for the presence of two components was 1.553 (95% CI: 1.540–1.567), the HR for the presence of three components was 2. Two hundred and fifty-six (95% CI: 2.235–2.277), the HR for the presence of four components was 2.487 (95% CI: 2.460–2.514), and the HR for the presence of five components was 2.605 (95% CI: 2.553–2.659).

A higher incidence of CV events was observed over approximately 10 years as the number of satisfied independent variables increased (Figure 2A). The COPD-/MetS- group had the highest proportion of participants without CV events,



Participants at risk:	2014	2015	2016	2017	2018	2019
COPD– / MetS–	3738458	3590516	3533516	3477076	3420817	3363151
COPD– / MetS+	1193014	1107303	1078545	1051449	1025250	999613
COPD+ / MetS–	125976	115273	111431	107963	104688	101607
COPD+ / MetS+	44362	38998	37238	35682	34278	32995

Participants at risk:	2014	2015	2016	2017	2018	2019
COPD– / MetS–	3738458	3700579	3684397	3667046	3648171	3627062
COPD– / MetS+	1193014	1176434	1169243	1161146	1152339	1142421
COPD+ / MetS–	125976	120362	118266	116000	113670	111274
COPD+ / MetS+	44362	42625	41976	41236	40434	39569

Participants at risk:	2014	2015	2016	2017	2018	2019
COPD– / MetS–	3738458	3732847	3730412	3727671	3724628	3721174
COPD– / MetS+	1193014	1190035	1188732	1187236	1185519	1183595
COPD+ / MetS–	125976	125317	125011	124684	124337	123955
COPD+ / MetS+	44362	44093	43978	43861	43728	43544

Figure 2 Kaplan–Meier survival analysis. (**A**) Cumulative CV events. (**B**) All-cause mortality. (**C**) Cardiovascular mortality.
Abbreviations: CV, cardiovascular; COPD, chronic obstructive pulmonary disease; +, disease exists; –, disease does not exist.

followed by the COPD-/MetS+ group (HR, 1.648; 95% CI, 1.640–1.656; P < 0.0001), COPD+/MetS- (HR, 1.993; 95% CI, 1.969–2.018; P<0.0001) and the COPD+/MetS+ group (HR, 2.740; 95% CI, 2.692–2.789; P < 0.0001).

The incidence of CV events per 1000 person-years increased in this order: COPD-/MetS-, 11.08; COPD-/MetS+, 20.44; COPD+/MetS-, 24.89; and COPD+/MetS+, 35.41. The COPD-/MetS+ and COPD+/MetS+ groups had the lowest and highest unadjusted HR, respectively (HR, 2.032, 95% CI, 2.484–2.545, P < 0.001 and HR, 3.777, 95% CI, 3.711–3.845, P < 0.001; Table 2). After initially adjusting for age and sex and after additional adjustment for smoking status and frequency of drinking alcoholic beverages, the risk of CV events in the COPD+/MetS+ group decreased but remained the highest among the groups (HR, 2.386, 95% CI, 2.344–2.429, P < 0.001 and HR, 2.368, 95% CI, 2.326–2.411, P < 0.001, respectively; see Table 2).

All-Cause Mortality Rate

The Results of the initial chi-squared analysis showed a trend of an increasing mortality rate during the outcome window with more independent variables, despite COPD being independently associated with the highest mortality rate (COPD-/MetS-: 4.2%; COPD-/MetS+: 6.1%; COPD+/MetS-: 15.5%; and COPD+/MetS+: 14.9%). The corresponding incidence per 1000 person-years was as follows: COPD-/MetS-: 3.89; COPD-/MetS+: 6.35; COPD+/MetS-: 16.95; and COPD +/MetS+: 17.04. A similar trend was observed for CV event-free survival, where the COPD-/MetS- group had the highest proportion of survivors during the outcome window, followed by the COPD-/MetS+ (HR, 1.372; 95% CI, 1.359–1.385; P < 0.0001) and COPD+/MetS+ (HR, 2.787; 95% CI, 2.713–2.863; P < 0.0001) groups. The COPD+/MetS- groups (HR, 2.866; 95% CI, 2.819–2.914; P < 0.0001) had the lowest percentage (Figure 2B).

A trend of increase in the unadjusted HR was observed with each additional independent variable, with COPD showing a stronger effect than MetS (Table 2). This trend persisted after adjusting for age and sex and after additionally adjusting for smoking status and frequency of drinking alcoholic beverages (see Table 2).

Incident Cardiovascular Mortality

The rate of mortality from a cardiovascular cause increased with each addition of an independent variable, and COPD had a stronger effect than MetS (COPD-/MetS-, 0.7%; COPD-/MetS+, 1.1%; COPD+/MetS-, 2.2%; and COPD+/MetS+, 2.6%). The incidence per 1000 person-years was 1.21, 1.40, 1.47, and 1.54 for the COPD-/MetS-, COPD-/MetS+, COPD +/MetS-, and COPD+/MetS+ groups, respectively.

Death-free survival related to cardiovascular causes showed the same trend with each additional independent variable. However, death-free survival during the outcome period decreased, and COPD showed a stronger effect as an independent variable than MetS (Figure 2C). The COPD-/MetS- group had the highest proportion of participants without cardiovascular mortality during the outcome window, followed by the COPD-/MetS+ (HR, 1.554; 95% CI, 1.519–1.589; P < 0.0001), COPD+/MetS- (HR, 2.571; 95% CI, 2.463–2.683; P < 0.0001), and the COPD+/MetS+ (HR, 2.881; 95% CI, 2.703–3.071; P < 0.0001) groups.

The initial crude HR of each group followed the trend observed in the Kaplan–Meier analysis, where the risk of mortality due to cardiovascular causes increased as the number of independent variables increased (the effect was stronger for COPD than for the MetS groups; Table 2). Additional adjustments to both models, as applied to Cox regression above, for cardiovascular mortality risk did not change the relationship between the number of independent variables and the risk (Table 2).

Discussion

In this study, we assessed the effects of COPD and MetS on CVD incidence and mortality using a large-scale population dataset from NHID. The major finding of this study was that the cumulative incidence of CV events, all-cause mortality rate, and cardiovascular mortality rate was significant when COPD and MetS coexisted. Concomitant COPD and MetS were associated with a significantly higher risk of adverse outcomes compared to either of them alone.

MetS is associated with higher risks of incidence of CV events, and all-cause and cardiovascular mortalities.[7] A nationwide, prospective cohort study conducted in China that followed the clinical course of 30,378 participants for 10 years reported an HR of 2.01 for CV events (ischemic heart diseases and stroke).[18] The study findings confirmed that,

after adjusting for confounding variables, the risks of all-cause and cardiovascular mortality were higher in individuals with MetS than in those without it. In our study population, 26.0% of patients with COPD had MetS, while 3.6% of patients with MetS had COPD. Even though COPD is less common in patients with MetS, we found higher rates of CV events and mortality in this group compared to those without COPD. Therefore, it may be important to identify the presence of COPD in patients with MetS.

In our study, the coexistence of COPD and MetS was associated with higher risks of CV event incidence and all-cause and cardiovascular mortalities than the presence of either COPD or MetS alone. Systemic inflammatory response may be a possible mechanism for the link between COPD and an increased risk of CV events.[1,2,4,19] According to this hypothesis, COPD-related chronic inflammation contributes to atherosclerotic plaque development, progression, and rupture, leading to acute cardiovascular events triggered by factors like respiratory tract infections or exacerbations.[20] Our results were similar to that of a previous study involving 11,493 patients with COPD and 22,986 controls, which showed increased risks of all-cause and cardiovascular mortality.[21]

Our study revealed that CV event incidence related to MetS was initially lower than those related to COPD, but the trend was reversed after adjusting for age and sex, possibly due to group age distribution. The MetS-only group had a higher proportion of younger participants than the COPD-only group, with their peak ages being within the 40s (34.2%); the peak ages of the COPD-only group were within the 60s (32.2%). Age is a significant risk factor for incident CV events. The incidence of atherothrombotic stroke[22] and coronary heart disease[23] increases with age in both men and women. Therefore, the reverse HR trends for MetS and COPD in our study may result from the age distribution difference between the groups.

Another possible explanation is that MetS is associated with incident CV events at a younger age than COPD. A cross-sectional study examining the influence of age on the prevalence of MetS and its association with CV events reported that the odds ratio (OR) for CV events in the MetS group was the highest for participants younger than 45 years (OR, 24.3; 95% CI, 2.4–241), and this relationship was not significant for participants older than 65 years (OR, 0.83; 95% CI, 0.37–1.87).[24] Therefore, it can be assumed that the effect of MetS on incident CV events was masked by our inclusion criteria for participants aged at least 40 years.

Both COPD and MetS are associated with systemic inflammatory response and physical inactivity.[8,25] The occurrence of comorbidities and complications such as CV events is amplified in patients with coexisting COPD and MetS.[3,8,26,27] Manglano et al showed an OR of 1.98 (P = 0.007) for heart failure and 1.67 (P = 0.09) for coronary artery disease for patients with COPD who had MetS relative to those who did not. This indicates that a higher risk of CV events is associated with the coexistence of COPD and MetS, despite the study being cross-sectional.[14]

The prevalence of MetS in the United States was 33% from 2003 to 2012 among adults aged ≥20 years based on the National Health and Nutrition Examination Survey (NHANES) data.[28] The prevalence in Korea was estimated at 28.9% in 2013 for adults aged ≥20 years based on the Korea NHANES data.[29] In our study of adults aged ≥40 years, the prevalence of MetS was 24.3%, which is similar to those reported by previous population-based studies. The global prevalence of COPD was estimated to be 10.3% for those aged 30–79 years in 2019.[30] The prevalence of COPD in Korea was reported at 13.4% for adults over the age of 40 years based on the Korea NHANES in 2015 using spirometry.[31] However, the prevalence of COPD diagnosed by physicians in a real-world study and the rate of treatment were only 2.8% and 1.6%, respectively, based on the questionnaire results at the time of spirometry.[31] Our study showed that the proportion of patients diagnosed with COPD who were taking medications was 3.3%. The lower prevalence of COPD in our study is thought to be associated with the lack of awareness regarding COPD.

This study has some limitations. First, this study used data from a cohort from the Korean population; therefore, it may not be representative of other populations. Second, the diagnoses of COPD, MetS, and CV events were based on operational definitions. Third, data on physical inactivity and FEV1 could not be obtained to classify the severity of COPD. Lastly, possible confounding factors may not have been ruled out, although potential confounders were adjusted for.

Conclusion

In Conclusion, both COPD and MetS independently increased the incidence and mortality of CV events. Additionally, when COPD and MetS coexisted, the effect was further increased. Despite the initial lower incidence of CV events in MetS compared to COPD, adjustments for age and sex revealed a reversal in the trend, potentially influenced by age distribution. Our findings provide crucial insights into the independent and combined effects of COPD and MetS on CV outcomes, offering valuable information for clinical management and preventive strategies.

Abbreviations

BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; DBP, diastolic blood pressure; FEV1, forced expiratory volume in 1 second; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; ICD-10, International Classification of Disease, tenth revision; ICSs, inhaled corticosteroids; LABAs, long-acting β2-agonists; LAMA, long-acting muscarinic antagonists; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; NHID, National Health Information Database; OR, odds ratio; SABA, short-acting β2-agonists; SAMA, short-acting muscarinic antagonists; SBP, systolic blood pressure; SD, standard deviation; TG, triglycerides.

Data Sharing Statement

Data were obtained from the National Health Information Database (NHID) and are available at http://nhiss.nhis.or.kr (accessed December 31, 2022). NHID allows access to all these data for any researcher who adheres to the research ethics at some cost. Those seeking access to this article's data can download it from the website after providing consent to follow the research ethics.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Board of Wonju Severance Christian Hospital (CR320340) and adhered to the principles of the Declaration of Helsinki. Anonymous and de-identified information was used for our study, and the requirement for informed consent was waived.

Author Contributions

All authors took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article was submitted; and agreed to be accountable for all the contents.

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Disclosure

The authors report no conflicts of interest in this work.

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