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Chronic obstructive pulmonary disease combined with vertebral compression fracture increases the risk of temporomandibular disorder

A population-based cohort study

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Abstract

Vertebral compression fracture (VCF) is a common comorbidity of chronic obstructive pulmonary disease (COPD), and the coexistence of COPD and temporomandibular disorder (TMD) has been clinically noted. The present study aimed to investigate whether VCF increases the risk of TMD in patients with COPD.

With a follow-up period of 15 years, this retrospective, population-based longitudinal cohort study enrolled sex- and age-matched COPD patients with and without VCF (1:3) who were identified from Taiwan's National Health Insurance Research Database from 2000 to 2015. Multivariate Cox regression analysis was performed to determine the risk of TMD in COPD patients with and without VCF. The cumulative risk of TMD between groups was estimated using Kaplan–Meier analysis.

The risk factors for TMD in patients with COPD were VCF, osteoporosis, and winter season. The COPD with VCF group was more likely to develop TMD (adjusted hazard ratio = 3.011, $P < .001$) than the COPD without VCF group after adjustment for sex, age, variables, and comorbidities. In the subgroup analysis, the COPD with VCF group had a higher risk of TMD than the COPD without VCF group in almost all stratifications.

COPD patients with VCF are at a higher risk of developing TMD. Clinicians taking care of patients with COPD should be aware of the occurrence of TMD as a comorbidity.

Abbreviations: BMD = bone mineral density, CCI = Charlson comorbidity index, CCI_R = Charlson comorbidity index revised, CI = Confidence interval, COPD = Chronic obstructive pulmonary disease, HR = Hazard ratio, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, NHIRD = National Health Insurance Research Database, TMD = Temporomandibular disorder, VCF = Vertebral compression fracture.

Keywords: chronic obstructive pulmonary disease, National Health Insurance Research Database, temporomandibular disorder, vertebral compression fracture

1. Introduction

Temporomandibular disorder (TMD) is a musculoskeletal condition characterized by pain and dysfunction in the temporomandibular joint and in the masticatory and facial muscles. The motor impairment symptoms associated with TMD include limited mandibular movement, painful mastication, and the presence of popping or clicking sounds during opening and closing of the mouth.[1] TMD is a multifactorial and concerning disease; however, only 15% of these patients seek medical treatment.[2] Female sex, anxiety, stress, rheumatoid arthritis, poor posture, and dysfunctional breathing are all risk factors contributing to TMD.[2–4] TMD is rarely present alone and is often associated with other comorbidities.[5]

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Chronic obstructive pulmonary disease (COPD) is characterized by progressive deterioration in pulmonary function and persistent airway inflammation.[6] Its symptoms include difficulty in breathing, coughing, mucus (sputum) production, and wheezing. Patients with COPD usually exhibit an upper chest breathing pattern and dyspnea on exertion.[7] Approximately 36% to 60% of patients with COPD have osteoporosis due to long-term glucocorticoid therapy; however, only a few patients are treated with bone-strengthening medications.[8,9]

As COPD severity progresses, the proportion of patients with osteoporosis increases. Osteoporosis is a systemic skeletal disease characterized by low bone mineral density and/or microarchitectural deterioration, resulting in increased bone fragility and hence, increased risk of fracture.[10] Severe osteoporosis will subsequently lead to vertebral compression fracture (VCF). VCF poses several medical problems, including back pain, thoracic kyphosis, and restricted pulmonary expansion.[11] Furthermore, VCF exacerbates dyspnea in patients with COPD, initiating a vicious cycle. Harrison et al[12] reported a reduction in vital capacity (range: 68–94% of predicted values) in patients with COPD owing to osteoporotic VCFs and the correlation between decline in pulmonary function and the degree of kyphosis. Kyphosis promotes forward head posture, and exacerbated dyspnea results in excessive neck accessory muscle firing.

The aforementioned factors may induce TMD, which impedes nutrition supplementation due to dysfunctional mastication.[13] Consequently, poor nutritional status leads to frailty and increases the mortality rates in patients with COPD. Previous studies have addressed the importance of nutritional support in patients with COPD; however, the occurrence of TMD in patients with COPD has rarely been discussed in previous studies.[14,15] Only Pinheiro et al[16] reported a high prevalence rate of TMD in patients with COPD. Moreover, we often found the coexistence of COPD and TMD in our clinical practice, especially in COPD patients with VCF. Therefore, this study aimed to investigate whether VCF increases the risk of TMD in patients with COPD and to compare the incidence of TMD between COPD patients with and without VCF who were identified from Taiwan's National Health Insurance Research Database (NHIRD).

2. Methods

2.1. Data sources and ethics

Data retrieved from the 2000 to 2015 Longitudinal Health Insurance Database, a subset of Taiwan's NHIRD, were used in this study to investigate the incidence of TMD between COPD patients with and without VCF over a 15-year period. The NHIRD comprises comprehensive data on disease diagnoses coded by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)[17]; treatments and procedures; service dates; patients' demographic characteristics; and drug prescriptions. The NHIRD is strictly used for research purposes, and all personally identifiable information is encrypted before being released to researchers to protect patient confidentiality. The National Health Insurance program was launched in Taiwan in 1995 and, as of June 2009, included contracts with 97% of healthcare providers with approximately 23 million beneficiaries or more than 99% of the entire population.[18] Several studies have shown the accuracy and validity of diagnoses in the NHIRD.[19,20] This study received approval from Tri-Service General Hospital (IRB No. 2-108-05-087), and the requirement for acquisition of informed consent from patients was waived.

2.2. Study design and sample population

A retrospective matched-cohort design was employed for this study. Patients diagnosed with COPD (ICD-9-CM codes 490–496) and consequent VCF of the thoracic and lumbar spines without traumatic spinal cord injury (ICD-9-CM codes 805.2, 805.4, 805.8) from 2000 to 2015 were assigned to the study group (Table 1).[21] Each enrolled COPD patient was required to have made at least three outpatient visits or one inpatient visit, but VCF diagnosis was made based on one outpatient or inpatient visit according to these ICD-9-CM codes. The date of the COPD and VCF diagnosis was defined as the index date. For each patient with COPD and VCF, 3 COPD patients without VCF, who were matched for sex, age, and index year, were allocated to the comparison group. A total of 12,012 COPD patients (study group, n = 3003; comparison group, n = 9009) were enrolled in this study. Both groups were followed from the index date until the onset of TMD or the end of 2015, and the diagnosis of TMD (ICD-9-CM code 524.6) was adapted from previous studies,[2,22,23] which were widely used in population studies. The flowchart of the study sample selection process is presented in Figure 1.

2.3. Exclusion criteria, comorbidities, and glucocorticoid intake

Patients diagnosed

1. with COPD, VCF, and TMD before 2000 (or prior to the first visit for TMD);
2. those with diseases that may involve the temporomandibular joint (details provided in Table 1); and
3. those aged < 20 years or >90 years and unknown sex were all excluded from the study.

Table 1

Diagnosis groups with corresponding ICD-9-CM codes.

Variables	ICD-9-CM
COPD	490–496
VCF	805.2, 805.4, 805.8
Events: TMD	524.6
Excluding	
1. Malignant neoplasm of the lip, oral cavity, and pharynx	140–149
2. Injuries on the head, face, or neck	800–804, 830, 941, 959.0
Comorbidities	
HTN	401–405
DM	250
CHF	428
Stroke	430–438
CKD	585–586
Migraine	346
Osteoporosis	733.0
Hyperlipidemia	272.0–272.4
Psychosis	295–299
Nonpsychotic mental disorders	300–314
Asthma	493
CAD	410–414
Insomnia	780.52
RA	714

CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, HTN = hypertension, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, RA = rheumatoid arthritis, TMD = temporomandibular disorder, VCF = vertebral compression fracture.

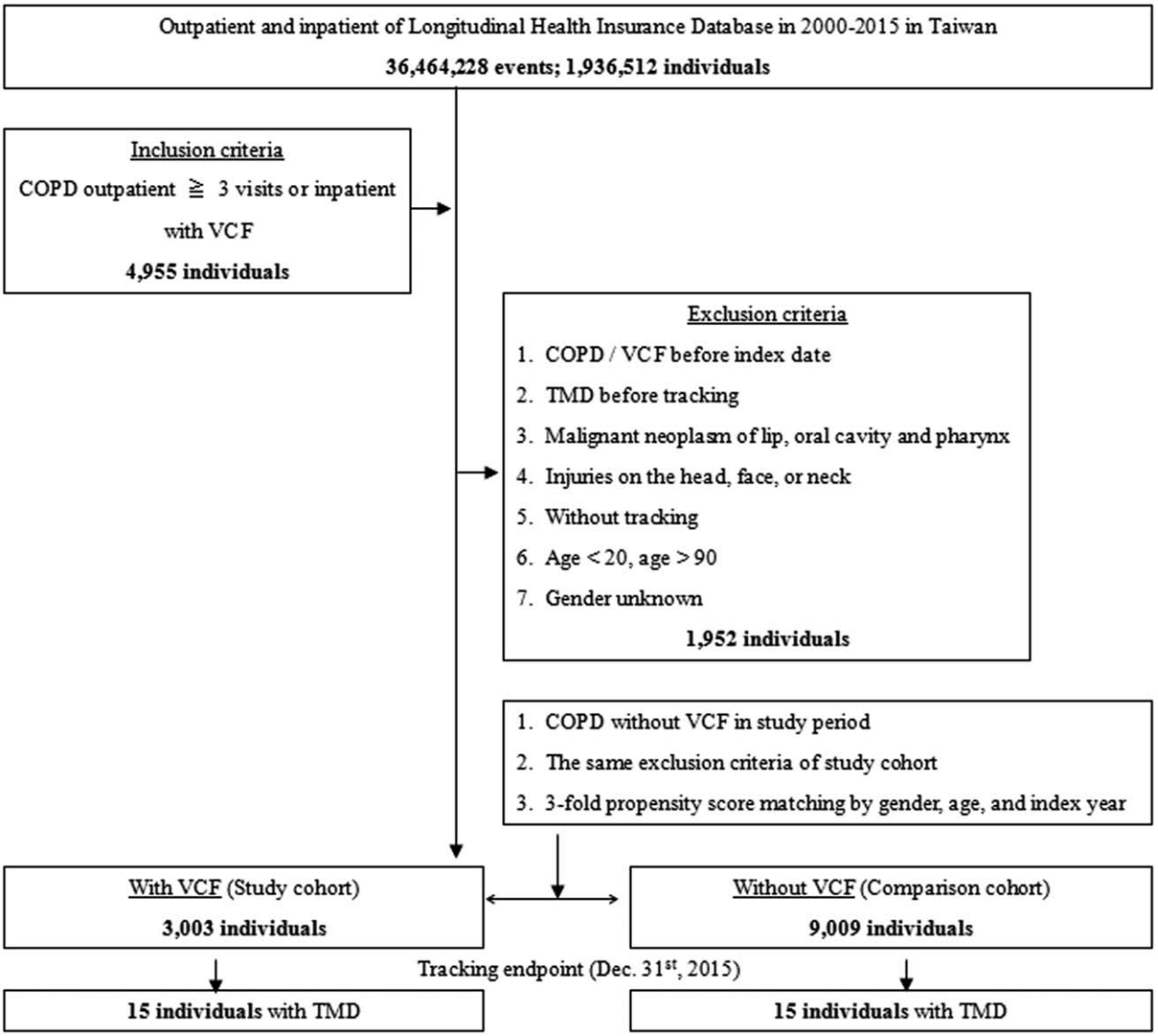

Figure 1. Flowchart of study sample selection process

Associated systemic diseases and risk factors for TMD were analyzed to compare the influence of these confounding factors between the two groups.[2–4] Comorbidities were identified using the ICD-9-CM diagnosis codes (Table 1). We also compared the risk of TMD development with and without glucocorticoid intake in COPD patients. The following glucocorticoid medications were analyzed: beclomethasone, budesonide, and fluticasone propionate.[24,25]

2.4. Statistical analysis

All analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY). The chi-square test and t-test were used to statistically examine the differences between the two cohorts. Multivariate Cox regression analysis was performed to determine the risk of TMD, with the analysis results presented as hazard ratio (HR) with 95% confidence interval (CI). The difference in the risk of TMD between the COPD with VCF group and the COPD without VCF group was estimated using Kaplan-Meier analysis with a log-rank test. A 2-tailed P value $< .05$ was considered statistically significant.

3. Results

3.1. Sample characteristics

The demographic characteristics of study participants are summarized in Table 2. No significant differences in sex, age, and insurance premium were observed between the COPD with VCF group and the COPD without VCF group. Furthermore, with respect to comorbidities, there were no significant differences in stroke, chronic kidney disease, migraine, hyperlipidemia, psychosis, nonpsychotic mental disorders, asthma, insomnia, rheumatoid arthritis, and Charlson comorbidity index revised (CCI_R) between the 2 groups. However, significant differences in season, level of care, hypertension, diabetes mellitus, congestive heart failure, osteoporosis, and coronary artery disease were noted between the 2 groups.

Table 2

Characteristics of the study and comparison group at baseline.

VCF	Study group With		Comparison group Without		
Variables	n	%	n	%	P
Total	3003	25.00	9,009	75.00	
Sex					.999
Male	1600	53.28	4,800	53.28	
Female	1403	46.72	4,209	46.72	
Age (years)	72.79 ± 8.51	71.61 ± 10.20	0.264		
Age group (years)					.999
40-49	42	1.40	126	1.40	
50-59	196	6.53	588	6.53	
60-69	312	10.39	936	10.39	
70-79	1521	50.65	4563	50.65	
80-90	932	31.04	2,796	31.04	
IP					.172
<18,000	2,965	98.70	8,885	98.62	
18,000–34,999	39	1.30	124	1.38	
Season					<.001
Spring	858	28.57	2,148	23.84	
Summer	702	23.38	1,742	19.34	
Autumn	506	16.85	1,625	18.04	
Winter	937	31.20	3,494	38.78	
Level of care					<.001
Hospital center	2418	80.52	5880	65.27	
Regional hospital	312	10.39	2041	22.66	
Local hospital	273	9.09	1088	12.08	
Comorbidities					
HTN	313	10.42	2,041	22.66	<.001
DM	199	6.63	1,145	12.71	<.001
CHF	77	2.56	672	7.46	<.001
Stroke	201	6.69	782	8.68	.721
CKD	41	1.37	117	1.30	.885
Migraine	1	0.03	15	0.17	.902
Osteoporosis	579	19.28	124	1.38	<.001
Hyperlipidemia	111	3.70	208	2.31	.792
Psychoses	13	0.43	66	0.73	.803
Nonpsychotic mental disorders	80	2.66	236	2.62	.881
Asthma	40	1.33	289	3.21	.385
CAD	164	5.46	1,512	16.78	<.001
Insomnia	7	0.23	79	0.88	.420
RA	2	0.07	22	0.24	.215
CCI_R	0.25 ± 1.07		0.24 ± 0.90		.872

CAD = coronary artery disease, CCI_R = Charlson comorbidity index revised, CHF = congestive heart failure, CKD = chronic kidney disease, DM = diabetes mellitus, HTN = hypertension, IP = insurance premium in New Taiwan dollars, RA = rheumatoid arthritis, VCF = vertebral compression fracture.

3.2. Kaplan-Meier analysis for the cumulative risk of TMD

The COPD with VCF group showed a significantly higher cumulative risk of TMD than the COPD without VCF group (log-rank $P < .001$). The cumulative risk of TMD became significantly different between the 2 groups since the second year of tracking (Fig. 2).

3.3. Factors for the incidence of TMD in Cox regression analysis

Cox regression analysis showed that the adjusted HR for the development of TMD was 3.011 times greater in the COPD with VCF group than in the COPD without VCF group (95% CI: 2.145–4.896, $P < .001$) after adjustment for demographic variables and comorbidities. Moreover, the risk factors contributing to the occurrence of TMD in patients with COPD were osteoporosis (adjusted HR = 9.000, $P < .001$) and winter season (adjusted HR = 3.401, $P = .002$), (Table 3).

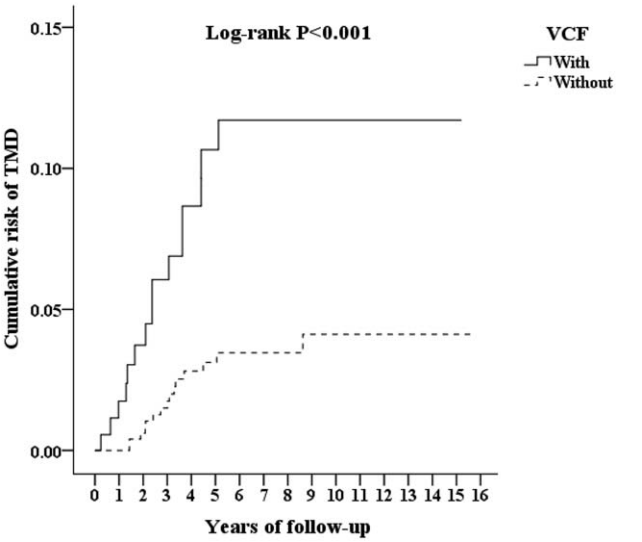

Figure 2. Kaplan–Meier analysis with log-rank test for the cumulative risk of TMD among patients with COPD aged 20 to 90 years, stratified by vertebral compression fracture.

3.4. Comparison of the risk of TMD stratified by glucocorticoid intake and VCF

In the subgroup analysis, we stratified patients by glucocorticoid intake and VCF. Compared to the patients without glucocorticoid intake, we found that COPD patients with glucocorticoid intake had a higher risk of TMD (adjusted HR = 2.596, $P < .001$) (Table 4). We compared the interactive effect of TMD occurrence between glucocorticoid intake and VCF. Each factor alone increased the risk of TMD; however, the combination of these 2 factors increased the risk of TMD substantially, much more than the sum of glucocorticoid intake and VCF (adjusted HR = 3.962, $P < .001$) (Fig. 3).

3.5. Risk of TMD between study group and comparison group stratified by variables and comorbidities

The COPD with VCF group had a higher event rate for TMD than the COPD without VCF group in almost all stratifications except local hospital care and absence of osteoporosis. Specifically, the COPD with VCF group patients stratified by age revealed that older patients had a higher risk for TMD (70–79-year-old age group: adjusted HR = 1.996, $P = .001$; 80–89-year-old age group: adjusted HR = 2.124, $P < .001$) than the COPD without VCF group (Table 5).

4. Discussion

Our results indicated that the overall adjusted HR for the occurrence of TMD in the COPD with VCF group was 3.011 (95% CI: 2.145–4.896, $P < .001$) after adjustment for sex, age, comorbidities, and other covariates. This means that COPD patients with VCF had a 3.011-fold increased risk of developing

Table 3

Factors for the incidence of temporomandibular disorder in Cox regression analysis.

Variables	Adjusted HR	95% CI	95% CI	*P*
VCF	3.011	2.145	4.896	<.001
Sex				
Male	1.972	0.465	6.470	.702
Female	Reference			
Age group (yr)				
50-59	0.000	–	–	.898
60-69	0.801	0.031	1.679	.942
70-79	0.376	0.095	1.602	.722
80-89	Reference			
IP				
<18,000	Reference			
18,000–34,999	0.000	–	–	.972
Season				
Spring	Reference			
Summer	1.295	0.592	1.862	.592
Autumn	0.892	0.201	1.304	.883
Winter	3.401	1.044	5.010	.002
Level of care				
Hospital center	2.006	1.000	7.892	.050
Regional hospital	1.101	0.503	3.342	.224
Local hospital	Reference			
Comorbidities				
HTN	1.822	0.703	2.775	.773
DM	1.514	0.484	2.876	.485
CHF	2.301	0.996	4.268	.055
Stroke	5.301	0.985	13.841	.061
CKD	1.498	0.935	2.597	.135
Migraine	-	–	–	–
Osteoporosis	9.000	3.010	48.603	<.001
Hyperlipidemia	0.000	–	–	.969
Psychoses	2.254	0.663	4.301	.389
Nonpsychotic mental disorders	1.986	0.423	3.984	.382
Asthma	1.765	0.894	2.986	.426
CAD	1.197	0.773	2.121	.333
Insomnia	0.000	–	–	.985
RA	0.000	–	–	.980

CAD = coronary artery disease, CHF = congestive heart failure, CI = confidence interval, CKD = chronic kidney disease, DM = diabetes mellitus, HR = hazard ratio, HTN = hypertension, IP = insurance premium in New Taiwan dollars, RA = rheumatoid arthritis, VCF = vertebral compression fracture.

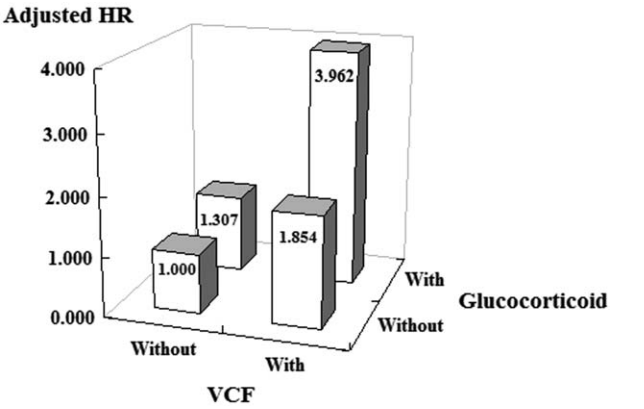

Figure 3. Comparison of the interactive risk of TMD stratified by vertebral compression fracture and glucocorticoid intake.

TMD compared to COPD patients without VCF. In addition, the cumulative risk for TMD occurrence between the two groups became significantly different from the second year of tracking. To the best of our knowledge, this is the first nationwide population-based cohort study with a follow-up period of 15 years to report the significant correlation between COPD with VCF and the occurrence of TMD.

Several studies have addressed the issues of malnutrition and poor appetite in patients with COPD which are associated with poor prognosis; TMD further exacerbates dysfunctional mastication.[14,26] However, there are only a few studies on TMD in patients with COPD. We report a high HR for TMD development in COPD patients with VCF. Hence, it is important to prevent dysfunctional mastication due to TMD in patients with COPD concurrent with VCF.

In this study, VCF, osteoporosis, and winter season were the risk factors contributing to the occurrence of TMD in COPD patients. Osteoporosis due to prolonged glucocorticoid use is a major comorbidity in patients with COPD.[8] Patients requiring oral glucocorticoid therapy have lower T-scores and more fractures than those treated with bronchodilators only. In addition, a 1.8-fold increased incidence of one or more vertebral fractures has been reported among patients receiving oral glucocorticoid therapy.[27]

Osteoporosis represents the most common etiology of VCFs which are known to result in impaired respiratory function via a reduction in thoracic mobility and postural deformity, particularly among patients with coexistent pulmonary disease, such as patients with COPD.[28] Restricted pulmonary expansion as a result of VCF in patients with COPD leads to an exacerbation of ventilatory distress, subsequently resulting in accessory muscle involvement to improve the change in air volume and increase muscular effort in the neck.[29,30] Both vital capacity and forced vital capacity are directly correlated with restrictive respiratory impairment.

A systematic review of osteoporosis-related kyphosis and impairment in pulmonary function reported that declines in vital capacity secondary to kyphosis seem modest and are directly related to the number of vertebral fractures and degree of kyphosis.[12] VCF may result in hyperkyphosis, leading to a concomitant reduction in vital capacity and forced expiratory volume in 1 second.[31] The symptoms of dyspnea worsen subsequent to postural change and volume reduction. Furthermore, excessive neck accessory muscle firing and forward head

Table 4

Comparison of the risk of temporomandibular disorder with and without glucocorticoid intake.

Glucocorticoid intake	Population size	Events (n)	Events (%)	ER	Adjusted HR	*P*
Without	7281	13	0.18	14.54	Reference	
With	4731	17	0.36	35.29	2.596	.023

ER = event rate per 10^5 person-years, HR = hazard ratio.

Table 5

Risk of temporomandibular disorder between study group and comparison group stratified by variables and comorbidities.

VCF Stratified	With Event	PYs	ER	Without Event	PYs	ER	With *vs.* Without Ratio	Adjusted HR	*P*
Total	15	32,304.37	46.43	15	105,282.69	14.25	3.259	3.011	<.001
Sex									
Male	8	13,751.96	58.17	8	68,254.42	11.72	4.963	4.585	<.001
Female	7	18,552.41	37.73	7	37,028.26	18.90	1.996	1.844	.002
Age group (yr)									
50-59	0	1,996.70	0.00	0	17,744.23	0.00	-	-	-
60-69	1	5,804.69	17.23	0	24,960.84	0.00	∞	∞	.895
70-79	5	12,743.71	39.24	7	38,551.59	18.16	2.161	1.996	.001
80-89	9	11,759.27	76.54	8	24,026.03	33.30	2.299	2.124	<.001
IP									
<18,000	15	31,268.67	47.97	15	104,883.64	14.30	3.354	3.011	<.001
18,000–34,999	0	1,035.70	0.00	0	399.04	0.00	-	-	-
Season									
Spring	4	13,691.94	29.21	3	23,494.24	12.77	2.288	2.114	<.001
Summer	7	9,293.40	75.32	6	21,558.06	27.83	2.706	2.500	<.001
Autumn	2	5,894.38	33.93	3	29,774.27	10.08	3.368	3.111	<.001
Winter	2	3,424.64	58.40	3	30,456.12	9.85	5.929	5.478	<.001
Level of care									
Hospital center	8	10,183.28	78.56	6	38,361.48	15.64	5.023	4.640	<.001
Regional hospital	5	14,102.75	35.45	4	45,154.42	8.86	4.002	3.698	<.001
Local hospital	2	8,018.34	24.94	5	21,766.79	22.97	1.086	1.003	.272
Comorbidities									
[0,1-10]HTN									
Without	13	26,512.98	49.03	14	85,103.68	16.45	2.981	2.754	<.001
With	2	5,791.39	34.53	1	20,179.00	4.96	6.969	6.438	<.001
[0,1-10]DM									
Without	12	28,158.22	42.62	13	90,870.10	14.31	2.979	2.752	<.001
With	3	4,146.15	72.36	2	14,412.59	13.88	5.214	4.817	<.001
[0,1-10]CHF									
Without	13	29,419.24	44.19	14	96,650.67	14.49	3.051	2.818	<.001
With	2	2,885.13	69.32	1	8,632.02	11.58	5.984	5.528	<.001
[0,1-10]Stroke									
Without	14	31,510.64	44.43	14	96,840.75	14.46	3.073	2.839	<.001
With	1	793.72	125.99	1	8,441.94	11.85	10.636	9.826	<.001
[0,1-10]CKD									
Without	10	31,153.98	32.10	10	100,129.28	9.99	3.214	2.969	<.001
With	5	1,150.39	434.64	5	5,153.41	97.02	4.480	4.139	<.001
[0,1-10]Migraine									
Without	15	32,304.37	46.43	15	105,282.69	14.25	3.259	3.011	<.001
With	0	0.00	-	0	0.00	-	-	-	-
[0,1-10]Osteoporosis									
Without	5	29,700.32	16.83	14	104,364.01	13.41	1.255	1.159	.198
With	10	2,604.05	384.02	1	918.68	108.85	3.528	3.259	<.001
[0,1-10]Psychoses									
Without	6	29,972.32	20.02	13	104,167.88	12.48	1.604	1.482	.036
With	9	2,332.04	385.93	2	1,114.81	179.40	2.151	1.987	.001
[0,1-10]Nonpsychotic mental disorders									
Without	6	31,146.27	19.26	13	104,722.70	12.41	1.552	1.434	.040
With	9	1,158.10	777.14	2	559.99	357.15	2.176	2.010	.001
[0,1-10]Asthma									
Without	12	31,431.12	38.18	14	104,257.69	13.43	2.843	2.627	<.001
With	3	873.25	343.54	1	1,025.00	97.56	3.521	3.253	<.001
[0,1-10]CAD									
Without	11	31,535.96	34.88	13	103,905.92	12.51	2.788	2.576	<.001
With	4	768.41	520.56	2	1,376.77	145.27	3.583	3.311	<.001
[0,1-10]Insomnia									
Without	15	30,977.81	48.42	15	102,863.41	14.58	3.321	3.011	<.001
With	0	558.15	0.00	0	1,042.51	0.00	-	-	-
[0,1-10]RA									
Without	15	32,304.36	46.43	15	104,775.94	14.32	3.243	3.011	<.001
With	0	0.01	0.00	0	506.75	0.00	-	-	-

CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, DM = diabetes mellitus, ER = event rate per 10^5 person-years, HR = hazard ratio, HTN = hypertension, IP = insurance premium in New Taiwan dollars, PYs = person-years, RA = rheumatoid arthritis, VCF = vertebral compression fracture.

posture may induce the symptoms of TMD.[32–34] Rodrigues Corrêa and Bérzin[7] reported the association between TMD and dysfunctional breathing, including mouth breathing syndrome, anxiety, changes in respiratory mechanics, diaphragmatic muscular dystonia, and overuse of accessory inspiratory muscles. Therefore, we can deduce that COPD with VCF can trigger the occurrence of TMD.

In the results of subgroup analysis stratified by glucocorticoid intake and VCF, COPD patients with glucocorticoid intake had a higher risk of TMD than without glucocorticoid. Previous studies[35,36] have demonstrated that inhaled glucocorticoids are associated with vertebral fractures in COPD patients. Moreover, glucocorticoid would worsen the progression of exist VCF in COPD patients and this could explain higher risk of TMD in COPD patients who had glucocorticoid intake and VCF simultaneously (adjusted HR = 3.962, $P < .001$) (Fig. 3). Patients with COPD in winter may be indicated for acute exacerbations, and respiratory distress may trigger the occurrence of TMD. A previous study also reported that exacerbations usually occur in patients with COPD during the cold season.[37]

The subgroup analysis stratified by sex, age, variables, and comorbidities revealed a higher risk of TMD in the COPD with VCF group than in the COPD without VCF group in almost all stratifications. The results demonstrated that VCF was a strong risk factor for TMD occurrence in patients with COPD. In the results of this present study, we must acknowledge that the incidence of TMD was higher among patients aged 70 to 89 years in the COPD population; however, this is not consistent with the general TMD prevalence.[38,39] Therefore, we cannot ignore the occurrence and importance of TMD in the elderly population with COPD because adequate nutrition intake is more critical for the elderly.

5. Limitations and strengths

The present study has some limitations. First, the actual prevalence of TMD might have been underestimated in the NHIRD because some symptoms associated with TMD are often observed in other diseases which create confusion or misdiagnosis. In addition, only a small proportion of patients with TMD seek medical treatment, and our data were derived from clinical diagnoses. Second, the event rate of TMD in our study was relatively low, and this may be due to the different sex distributions in the COPD and TMD groups. In contrast with male dominance among patients with COPD, strong female dominance was observed among patients with TMD.[40,41] However, we cannot ignore the high adjusted HR of 3.011, even if the event rate is low, as the low event rate cannot explain this value. Third, pulmonary function test or laboratory data, such as the score of bone mineral density, were not recorded in the database; therefore, the severity of COPD and osteoporosis could not be identified. Thus, we considered the most severe COPD patients to undergo treatment in the hospital center and the mildest COPD patients to undergo treatment in the local hospital. In Table 3, the results revealed that the risk of TMD development was highest in hospital centers (adjusted HR = 2.006) and moderate in regional hospitals (adjusted HR = 1.101) compared to local hospitals. Moreover, the diagnosis of osteoporosis was confirmed only when the bone mineral density was 2.5 standard deviations below the mean for adults, and the risk of TMD in COPD patients with osteoporosis was much higher than in those without osteoporosis (adjusted HR = 9.000, $P < .001$). Therefore, we should be aware of the occurrence of TMD even in COPD patients with mild osteoporosis.

Moreover, a major strength of our study is that using data based on a clinical diagnosis enabled reliable cohort assessment. Furthermore, our longitudinal cohort study could overcome the major limitation of cross-sectional and case-control study designs by only providing information on disease incidence.

In conclusion, TMD is more likely to occur as a comorbidity in COPD patients with VCF. Therefore, it is important to be aware of the occurrence of TMD when taking care of COPD patients, especially those with long-term glucocorticoid intake.

Author contributions

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