Original Article

Influence of Comorbidities on Hospital Mortality and Healthcare Utilization in Hospitalized Chronic Obstructive Pulmonary Disease Patients

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Background: Comorbidities of chronic obstructive pulmonary disease (COPD) are associated with both increased short-term and long-term mortality. However, information on regarding the influence of comorbidities on hospital mortality and healthcare utilization remain limited.

Objective: To evaluate the influence of COPD and comorbidities associated with increased risk of hospital mortality and healthcare utilization.

Materials and Methods: A retrospective cohort study was performed on COPD patients admitted to the Chiang Mai University Hospital between 2007 and 2013. Logistic regression was performed to identify independent comorbidities that increased the risk of hospital mortality and influenced healthcare utilization.

Results: The present study involved 739 COPD patients with 1,099 visits. The hospital mortality rate was 12.3%. The comorbidities associated with increased hospital mortality were depression (odds ratio [OR] 8.61, 95% confidence interval [CI] 1.66 to 43.95, p=0.010), atrial fibrillation (OR 2.37, 95% CI 1.33 to 4.21, p=0.003), and coronary artery disease (OR 1.85, 95% CI 1.03 to 3.32, p=0.04). The comorbidities were also associated with increased hospital length of stay [7 (3 to 12) versus 5 (3 to 8) days, p=0.001], mechanical ventilation days [5 (2 to 13) versus 3 (2 to 6) days, p=0.029], and total hospital costs [915.1 (401.2 to 2,258.4) versus 562.1 (338.1 to 1,372.9) USD, p=0.010]. In addition, comorbidities were associated with increased hospital mortality (one and two comorbidities: OR 2.06, 95% CI 1.24 to 3.43, p=0.005 and OR 5.47, 95% CI 2.07 to 14.47, p=0.001, respectively).

Conclusion: The COPD comorbidities, which are depression, atrial fibrillation, and coronary artery disease, were associated with increased hospital mortality and healthcare utilization.

Keywords: COPD, Comorbidity, Mortality, Healthcare utilization

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Chronic obstructive pulmonary disease (COPD), a chronic inflammatory airway disease, is an important cause of morbidity and mortality worldwide. Currently, COPD is the fourth leading cause of death in the world and is projected to be the third leading cause of death by 2020[1]. More than three million people died of COPD in 2012 accounting for 6% of all deaths globally[2]. In Chiang Mai, Northen Thailand, the prevalence of COPD in rural and urban groups was 6.8% and 3.7%, respectively[3]. In Thailand, according to the Bureau of epidemiology, Department of disease control, the prevalence of COPD was estimated at 176.77 per 100,000 populations in 2013.

For these reasons, COPD represents an important worldwide public health challenge, including in Thailand. Nevertheless, it can be preventable and treatable.

COPD patients frequently suffer from concurrent comorbidities such as cardiovascular disease[4], cerebrovascular disease[5], lung cancer[6], and

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diabetes[7]. Divo et al[8] recently reported that 15 of 79 comorbidities were related to an increase in long-term mortality during a median follow-up of 51 months. Almagro et al[9] reported data from the European Society for Molecular Imaging (ESMI) study, longitudinal, observational, multicenter study in hospitalized COPD patients that the comorbidities, which have an impact on short-term mortality (three months), were ischemic heart disease, heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic kidney disease, depression, and atrial fibrillation (AF).

Besides an increased mortality rate, COPD patients with comorbidities were associated with higher healthcare utilization, including length of stay and total cost compared with no comorbidity[10,11].

As mentioned above, comorbidities of COPD are associated with both increased short-term and long-term mortality. However, information on the influence of comorbidities on hospital mortality and healthcare utilization in Thailand remain limited, especially in high prevalence of COPD as Northern part of Thailand. The authors aimed to evaluate the influence of comorbidities associated with an increased risk of hospital mortality and healthcare utilization in hospitalized COPD patients.

Materials and Methods

Study design and participants

A retrospective cohort study was conducted in a 1,400-bed, tertiary care university hospital located in Northern Thailand. COPD patients hospitalized with acute exacerbation of COPD (AECOPD) and pneumonia that recorded in hospital database between 2007 and 2013 were included.

Inclusion and exclusion criteria

All COPD patients were diagnosed by spirometric criteria, post-bronchodilator FEV1/FVC ≤0.7 according to the GOLD guidelines, or physician diagnosis plus signs and symptoms suggesting COPD included at least one of the following: chronic cough, wheezing, Barrel-shaped chest from physical examination, imaging study presented with emphysematous changes, and finding as cor pulmonale from echo or EKG. The COPD patients were included if they were admitted into the Chiang Mai University Hospital between 2007 and 2013 due to AECOPD or pneumonia and the age at the onset of respiratory symptoms was 40 years or older. The patients were excluded from the study if the age at the onset of respiratory symptom was less than 40 years, or if they had a history of asthma or asthma-COPD overlap syndrome or other diagnosis that mimics COPD such as bronchiectasis.

Data collections

Demographic and clinical data were reviewed from the medical records and included age, gender, spirometry results, history of smoking and smoking status, clinical and physical examination, chest films, and reason for admission (categorized as AECOPD, pneumonia, other). Comorbidities were classified by the Charlson comorbidity index[12] and the COPD comorbidity index (COPD specific comorbidity test [COTE])[8] and included hospital mortality and healthcare utilization i.e., mechanical ventilator day, intensive care unit (ICU) length of stay, hospital length of stay, and total hospital cost.

The present study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University (EC no.456/2014).

Statistical analysis

Demographic data were expressed using descriptive statistics. Categorical data were expressed as absolute frequencies and percentages. Continuous variables were expressed as mean and standard deviation (SD), or as median and interquartile range (IQR). Group comparison was conducted using Fisher exact test, for categorical variables and two-tailed t-tests or the Wilcoxon rank-sum test, for continuous variables.Univariable and multivariable logistic regression analysis with age adjusted as confounding factors was performed to identify independent comorbidities that increased the risk of hospital mortality and influence healthcare utilization. Each variable with a p-value of less than 0.05 in the univariable analysis was considered a factor to be analyzed later in the multivariable model to define the final independent factors. A p-value of less than 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics software, version 20.0 (IBM Corp., Armonk, NY, USA) and Stata, version 12 (StataCorp LP, College Station, TX, USA).

Results

Seven hundred thirty-nine COPD patients with 1,099 admissions were enrolled in the study. The admission causes were AECOPD (800 admissions, 72.8%) and pneumonia (299 admissions, 27.2%) as shown in Figure 1.

The baseline characteristics and cause of

Table 1. Baseline characteristics of hospitalized COPD patients

Variables	Without comorbidity (n=179) n (%)	With comorbidity (n=560) n (%)	p-value
Sex: male	113 (63.1)	316 (56.4)	0.114
Age (year); mean±SD	69.8±10.1	74.2±9.7	<0.001
Barrel chest	24 (13.4)	49 (8.8)	0.050
Emphysematous	77 (43.0)	187 (33.4)	0.019
Cor pulmonale	32 (17.9)	96 (17.1)	0.821
Cause of admission			0.479
AECOPD	126 (70.4)	379 (67.7)	
Pneumonia	53 (29.6)	181 (32.3)	

AECOPD=acute exacerbation of chronic obstructive pulmonary disease; SD=standard deviation

Table 2. Comorbidities of COPD patients among survivor and non-survivor group

Variables	Total (n=739) n (%)	Survivor (n=648) n (%)	Non-survivor (n=91) n (%)	p-value
Hospital mortality			91 (12.3)	
Cardiovascular disease	426 (57.6)	366 (56.5)	60 (65.9)	0.087
Atrial fibrillation	86 (11.6)	67 (10.3)	19 (20.9)	0.002
Congestive heart failure	99 (13.4)	83 (12.8)	16 (17.6)	0.180
Coronary artery disease	91 (12.3)	73 (11.3)	18 (19.8)	0.016
Cerebrovascular disease	63 (8.5)	56 (8.6)	7 (7.7)	0.829
Hypertension	337 (45.6)	294 (45.4)	43 (47.3)	0.537
Malignancy	53 (7.2)	46 (7.1)	7 (7.7)	0.777
Diabetes	89 (12.0)	73 (11.3)	16 (17.6)	0.063
Peptic ulcer	14 (1.9)	10 (1.5)	4 (4.4)	0.077
Chronic liver disease	15 (2.0)	14 (2.2)	1 (1.1)	0.522
Chronic kidney disease	86 (11.6)	73 (11.3)	13 (14.3)	0.400
Osteoporosis	16 (2.2)	14 (2.2)	2 (2.2)	0.949
Dyslipidemia	93 (12.6)	79 (12.2)	14 (15.4)	0.330
Depression	6 (0.8)	3 (0.5)	3 (3.3)	0.004
Dementia	12 (1.6)	12 (1.9)	0 (0.0)	0.197
Rheumatologic disease	3 (0.4)	2 (0.3)	1 (1.1)	0.254
AIDS	1 (0.1)	1 (0.2)	0 (0.0)	0.712

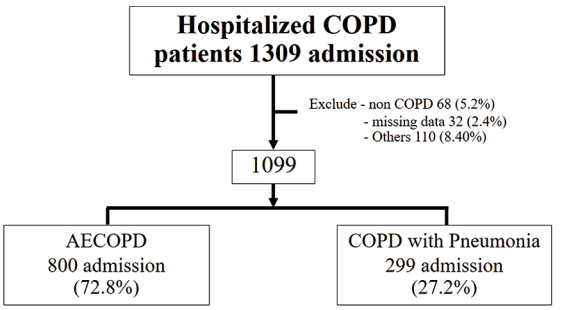

Figure 1. Data collection flow chart.

admission of 739 patients included in the analysis are summarized in Table 1. The number of patients with comorbidities was 560 (75.78%). There were statistically significant difference in the mean age (74.2±9.7 years versus 69.8±10.1 years, p<0.001), and emphysematous change in chest film 187 (33.4%) versus 77 (43%), p=0.019) between the comorbidity groups and without comorbidity group but no significant difference in gender, barrel chest, cor pulmonale and cause of admission.

From Table 2, the comorbidities collected in the

Table 3. Influence of comorbidities on mortality by univariable logistic regression

Predictor	Crude OR	95% CI	p-value
Cardiovascular disease	1.49	0.94 to 2.36	0.089
Atrial fibrillation	2.39	1.35 to 4.21	0.003
Coronary artery disease	2.00	1.13 to 3.54	0.018
Congestive heart failure	1.50	0.83 to 2.69	0.182
Cerebrovascular disease	0.91	0.40 to 2.07	0.829
Hypertension	1.15	0.74 to 1.80	0.537
Malignancy	1.13	0.49 to 2.58	0.777
Diabetes	1.75	0.96 to 3.16	0.066
Peptic ulcer	3.00	0.92 to 9.80	0.068
Chronic kidney disease	1.31	0.69 to 2.48	0.401
Osteoporosis	1.05	0.23 to 4.70	0.949
Dyslipidemia	1.36	0.73 to 2.52	0.332
Depression	7.48	1.48 to 37.6	0.015
Rheumatologic disease	3.70	0.33 to 41.2	0.287
Charlson index	1.11	0.99 to 1.24	0.077
COTE	1.17	1.03 to 1.32	0.014

COTE=comorbidity test; OR=odds ratio; CI=confidence interval

Table 4. Influence of comorbidities on mortality by multivariable logistic regression

Predictor	Adjusted OR	95% CI	p-value
Atrial fibrillation	2.37	1.33 to 4.21	0.003
Coronary artery disease	1.85	1.03 to 3.32	0.040
Depression	8.61	1.66 to 43.95	0.010
No. of comorbidities			
0	Reference		
1	2.06	1.24 to 3.43	0.005
2	5.47	2.07 to 14.47	0.001

OR=odds ratio; CI=confidence interval

present study included five cardiovascular diseases (AF, congestive heart failure, coronary artery disease [CAD], cerebrovascular disease, and hypertension). Three comorbidities, which are AF, CAD, and depression, had a significant increase in the non-survivor group [10.3% versus 20.9% (p=0.002), 11.3% versus 19.8% (p=0.016) and 0.5% versus 3.3% (p=0.004), respectively]. There were no significant differences in the other comorbidities.

The logistic regression analyses were conducted between hospital mortality and the comorbidities as shown in Table 3. From the results of the univariable analyses (Table 3), the comorbidities that increased

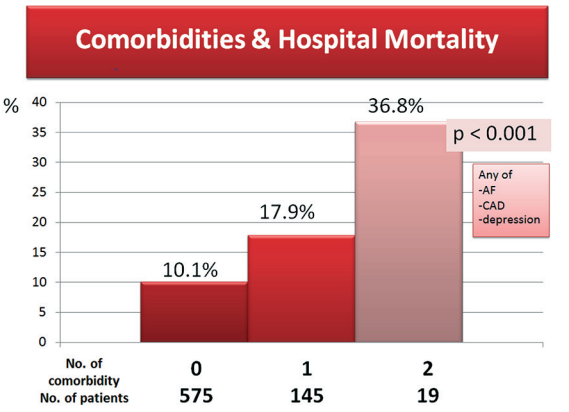

Figure 2. Number of comorbidities associated with hospital mortality.

There were no patients in the study who had all 3 comorbidities (atrial fibrillation [AF], coronary artery disease (CAD), and depression).

risk of hospital mortality in COPD patients were depression (odds ratio [OR] 7.48, 95% confidence interval [CI] 1.48 to 37.6, p=0.015), AF (OR 2.39, 95% CI 1.35 to 4.21, p=0.003) and CAD (OR 2.00, 95% CI 1.13 to 3.54, p=0.018). Additionally, every one-point increase of the COTE index was associated with an increase in the hospital mortality by 17% (OR 1.17, 95% CI 1.03 to 1.32, p=0.014).

The multivariate analyses between hospital mortality and the significant comorbidities from univariable logistic analysis are shown in Table 4. Depression (OR 8.61, 95% CI 1.66 to 43.95, p=0.010), AF (OR 2.37, 95% CI 1.33 to 4.21, p=0.003), and CAD (OR 1.85, 95% CI 1.03 to 3.32, p=0.04) were still significantly associated with increasing of hospital mortality. In addition, the number of those comorbidities (depression, AF, and CAD) were associated with an increase in the non-survivor group (2 versus 1 versus no comorbidities were 36.8% versus 17.9% versus 10.1%, respectively, p<0.001) (Figure 2). However, no patients in the present study had the three comorbidities. The patients with one and two comorbidities had a significant increase in hospital mortality (OR 2.06, 95% CI 1.24 to 3.43, p=0.005 and OR 5.47, 95% CI 2.07 to 14.47, p=0.001, respectively) compared with none of depression, AF, and CAD (Table 4).

According to the healthcare utilization (Figure 3), the comorbidities were also associated with increases in hospital lengths of stay [7 (3 to 12) versus 5 (3 to 8) days, p=0.001], mechanical ventilation days [5 (2 to 13.7) versus 3 (2 to 6) days, p=0.029], and total hospital cost [29,284 (12,838 to 72,269) versus 17,988

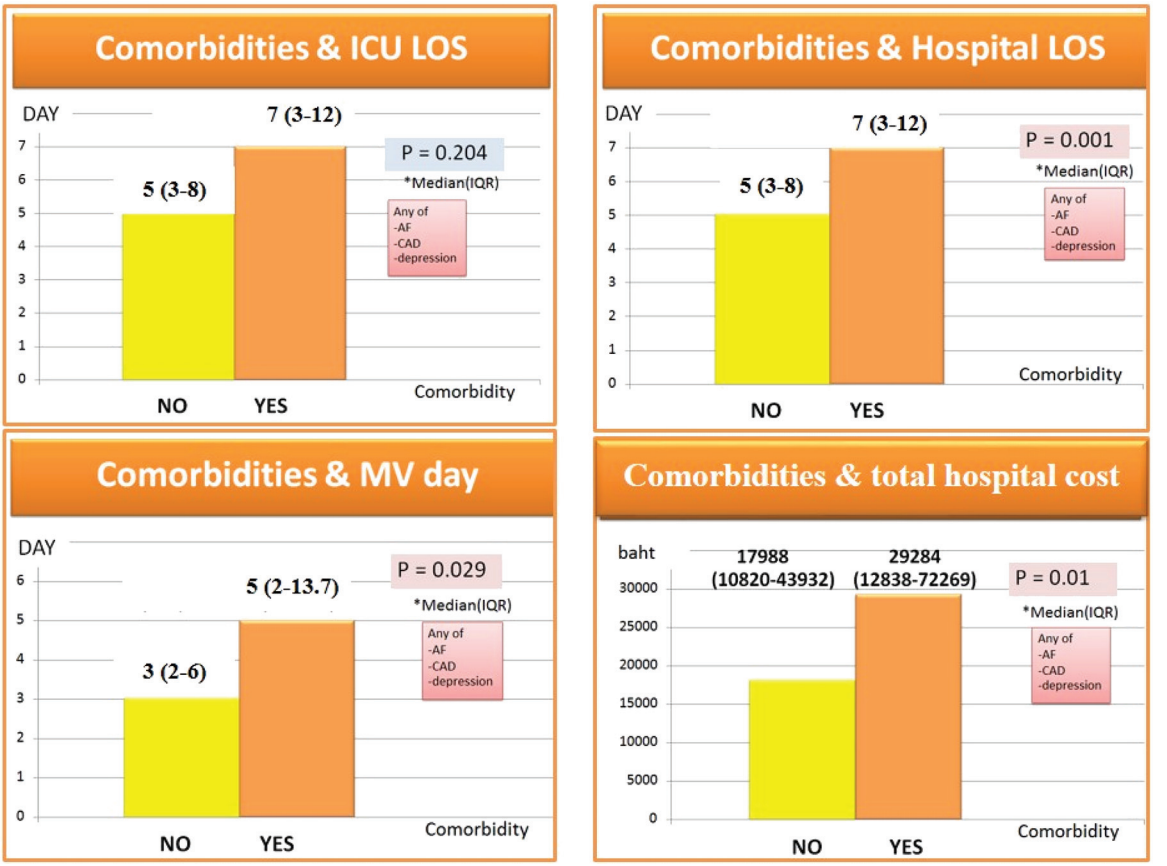

Figure 3. Presence of comorbidities associated with healthcare utilization.

ICU LOS=length of stay in intensive care unit, Hospital LOS=length of stay in hospital, MV day=mechanical ventilator day, Currency exchange rates 1 USD=32 Thai Baht (average rate in Aug 2014)

(10,820 to 43,932) Thai Baht, p=0.010] (Rate 32.0 Thai Baht/1USD, average in Aug 2014).

Discussion

In the present study identified the comorbidities associated with increased risk of hospital mortality in hospitalized COPD patients with AECOPD or pneumonia. The significant comorbidities were CAD, AF, and depression.

COPD is frequently found in combination with CAD. Both share the same main risk factors, which are smoking and inflammatory diseases[13]. Two large studies of administrative datasets have estimated the prevalence of CAD among patients with COPD to be 22% to 33.6%[14,15]. Donaldson et al[16] showed that the risk of acute vascular events appeared to be particularly high during AECOPD. After analyzing the data from 25,857 patients with COPD entered in the Health Improvement Network Database over a 2-year period, they found that the risk of myocardial infarction (MI) one to five days after exacerbation increased 2.3-fold. From the present study data, hospitalized COPD patients with CAD had a high risk of hospital mortality (OR 1.85, 95% CI 1.03 to 3.32, p=0.04). This may be associated with acute MI after AECOPD. In addition, from a previous study[9], CAD was also associated with an increased risk of three-month mortality in hospitalized COPD patients (OR 1.29, 95% CI 1.04 to 1.61, p<0.01).

COPD was associated with an increased likelihood of atrial flutter/AF (23.3% versus 11.0%, p<0.001)[17]. In 2012, Steer et al[18] showed that the Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation (DECAF) score was used as a predictor of mortality in hospitalized patients with COPD exacerbations. The DECAF score consisted of the five strongest predictors of mortality, including AF that were associated with an increased risk of hospital mortality (OR 2.66, 95% CI 1.39 to 5.09, p=0.003). In the present study, AF was found at

11.6% and associated with increased risk of hospital mortality (OR 2.365, 95% CI 1.33 to 4.21, p=0.003). Smoking, airway inflammation, hypoxia, hypercapnia, pulmonary hypertension, β-adrenergic agonist, and steroids, found in hospitalized COPD patients, all contributed to ultimately causing or worsening AF[19] and might be causing higher mortality rates in COPD patients with AF.

The prevalence of depression in moderate-to-severe COPD patients in a previous study ranged from 7% to 42%[20]. However, the prevalence of depression in the present study was 0.8%. Depression might be under-diagnosed by physicians. Evidence from a previous study showed that depression associated with increased risk of three-month (OR 3.24, 95% CI 1.02 to 10.1, p<0.01)[9] and one-year mortality (hazard ratio [HR] 1.93; 95% CI 1.04 to 3.58)[21] in hospitalized COPD patients. In addition, depression in the present study was still associated with increased risk of hospital mortality (OR 8.61, 95% CI 1.66 to 43.95, p=0.010). Depression may influence decisions related to end-of-life issues, issues of informed consent, and capacity to understand the consequences of accepting or refusing treatment.

It was not surprising that the number of those comorbidities (depression, AF, and CAD) were associated with an increase in mortality rates (2 versus 1 versus no comorbidities at 36.8% versus 17.9% versus 10.1%, respectively, p<0.001). In addition, the patients with one and two comorbidities had a significantly increased hospital mortality (OR 2.06, 95% CI 1.24 to 3.43, p=0.005 and OR 5.47, 95% CI 2.07 to 14.47, p=0.001, respectively) compared with non- comorbidity. However, there were no patients in the present study had the three comorbidities. Several studies have demonstrated an increased risk of death in individuals with COPD and multiple comorbidities[8,11]. Divo et al noted significant increases in risk for death in individuals with higher values of the COTE index (HR 1.13, 95% CI 1.08 to 1.18)[8]. The present study also showed that higher scores of the COTE index were associated with an increase in hospital mortality (OR 1.17, 95% CI 1.03 to 1.32, p=0.014).

With regard to healthcare utilization, the present study showed that the patients with one of those comorbidities were significantly associated with higher hospital lengths of stay [7 (3 to 12) versus 5 (3 to 8) days, p=0.001], mechanical ventilation days [5 (2 to 13) versus 3 (2 to 6) days, p=0.029], and total hospital cost [29,284 (12,838 to 72,269) versus 17,988 (10,820 to 43,932 Baht, p=0.010] or [915.1 (401.2 to 2,258.4) versus 562.1 (338.1 to 1,372.9) USD], (1 USD=32 Thai Baht, average rate in Aug 2014). Similarly, the analysis of the Finnish administrative hospitalization data showed that among hospitalizations in which COPD was the primary diagnosis, the presence of other diagnoses was associated with significantly longer length of hospitalization[10]. Additionally, one study of the Maryland Medicaid Claims showed that, among individuals with COPD, the presence of comorbidities was associated with significantly higher health expenditures[22].

The present study strength was that the authors studied from a large database of COPD in a tertiary care, university hospital. As a result, it can be applicable to real life practice. However, there were some limitations. Firstly, the present study was a retrospective cohort conducted in a single university hospital, the data, thus, may not be applicable in the different settings such as community hospitals. Secondly, some comorbidities such as depression may be underdiagnosed by physicians.

Therefore, the authors suggested that the study should be done in other settings such as in primary care hospitals along with a prospective cohort.

Conclusion

COPD comorbidities i.e., depression, AF, and CAD were associated with increased hospital mortality and healthcare utilization. Physicians should look for those comorbidities in every COPD patient hospitalized with AECOPD or pneumonia.

What is already known on this topic?

COPD patients with comorbidities have increased mortality and associated with higher healthcare utilization varied by countries.

What this study adds?

In Thailand, COPD comorbidities with depression, AF, and coronary artery disease were associated with increased hospital mortality and healthcare utilization.

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Conflicts of interest

The authors declare no conflicts of interest in this study.

References

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095-128.
2. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease. Global Initiative for Chronic Obstructive Lung Disease (GOLD) [Internet]. 2017 [cited 2020 Apr 20]. Available from: https://goldcopd.org/.
3. Pothirat C, Chaiwong W, Phetsuk N, Pisalthanapuna S, Chetsadaphan N, Inchai J. A comparative study of COPD burden between urban vs rural communities in northern Thailand. Int J Chron Obstruct Pulmon Dis 2015;10:1035-42.
4. Anthonisen NR, Connett JE, Enright PL, Manfreda J. Hospitalizations and mortality in the Lung Health Study. Am J Respir Crit Care Med 2002;166:333-9.
5. Hansell AL, Walk JA, Soriano JB. What do chronic obstructive pulmonary disease patients die from? A multiple cause coding analysis. Eur Respir J 2003;22:809-14.
6. Mannino DM, Aguayo SM, Petty TL, Redd SC. Low lung function and incident lung cancer in the United States: data From the First National Health and Nutrition Examination Survey follow-up. Arch Intern Med 2003;163:1475-80.
7. Mannino DM, Thorn D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. Eur Respir J 2008;32:962-9.
8. Divo M, Cote C, de Torres JP, Casanova C, Marin JM, Pinto-Plata V, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;186:155-61.
9. Almagro P, Cabrera FJ, Diez-Manglano J, Boixeda R, Recio J, Mercade J, et al. Comorbidome and short-term prognosis in hospitalised COPD patients: the ESMI study. Eur Respir J 2015;46:850-3.
10. Kinnunen T, Saynajakangas O, Tuuponen T, Keistinen T. Impact of comorbidities on the duration of COPD patients' hospital episodes. Respir Med 2003;97:143-6.
11. Budweiser S, Harlacher M, Pfeifer M, Jorres RA. Co-morbidities and hyperinflation are independent risk factors of all-cause mortality in very severe COPD. COPD 2014;11:388-400.
12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
13. Boschetto P, Beghe B, Fabbri LM, Ceconi C. Link between chronic obstructive pulmonary disease and coronary artery disease: implication for clinical practice. Respirology 2012;17:422-31.
14. Mapel DW, Dedrick D, Davis K. Trends and cardiovascular co-morbidities of COPD patients in the Veterans Administration Medical System, 1991-1999. COPD 2005;2:35-41.
15. Mapel DW, Hurley JS, Frost FJ, Petersen HV, Picchi MA, Coultas DB. Health care utilization in chronic obstructive pulmonary disease. A case-control study in a health maintenance organization. Arch Intern Med 2000;160:2653-8.
16. Donaldson GC, Hurst JR, Smith CJ, Hubbard RB, Wedzicha JA. Increased risk of myocardial infarction and stroke following exacerbation of COPD. Chest 2010;137:1091-7.
17. Konecny T, Park JY, Somers KR, Konecny D, Orban M, Soucek F, et al. Relation of chronic obstructive pulmonary disease to atrial and ventricular arrhythmias. Am J Cardiol 2014;114:272-7.
18. Steer J, Gibson J, Bourke SC. The DECAF Score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. Thorax 2012;67:970-6.
19. Shah V, Desai T, Agrawal A. The association between chronic obstructive pulmonary disease (COPD) and atrial fibrillation: a review. Open Access 2016;1:1-5.
20. van Ede L, Yzermans CJ, Brouwer HJ. Prevalence of depression in patients with chronic obstructive pulmonary disease: a systematic review. Thorax 1999;54:688-92.
21. Ng TP, Niti M, Tan WC, Cao Z, Ong KC, Eng P. Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. Arch Intern Med 2007;167:60-7.
22. Lin PJ, Shaya FT, Scharf SM. Economic implications of comorbid conditions among Medicaid beneficiaries with COPD. Respir Med 2010;104:697-704.