Original article

Hospitalization of patients with acute exacerbation of chronic obstructive pulmonary diseases in Sarapee Hospital: A retrospective study of prevalence and associated factors

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Objective To determine the prevalence of hospitalization of patients with acute exacerbation of chronic obstructive pulmonary diseases (AECOPD) and the association with COPD severity, co-morbidities, and treatment options.

Methods A retrospective study was conducted with 277 acute exacerbation COPD patients who were diagnosed and treated at Sarapee Hospital between October 2015 and September 2016. The primary outcome was the hospitalization due to acute exacerbation during the year of study.

Results Among the AECOPD patients treated at Sarapee Hospital, 21.3% were hospitalized. Predictors of the severity of the disease associated with hospitalization were found to including GOLD (Global Initiative for Obstructive Lung Disease) grade, steroid use, and home oxygen use. Of these three factors, home oxygen therapy was the strongest predictor (aOR=21.61, 95% CI=8.92- 52.38, p<0.001). Patients with ischemic heart disease (IHD) tended to have a higher rate of hospitalization for AECOPD than those with other co-morbidities (aOR=2.59, 95% CI=0.89-7.51, p-value 0.078). We found no statistically significant correlation with the other variables tested.

Conclusion Hospitalization for AECOPD was associated with home oxygen use and tended to be associated with IHD. Awareness of means of prevention of disease progression, including proper treatment and comorbid disease control, could potentially decrease the prevalence of hospitalization for AECOPD. Proper use of home oxygen should be further investigated. **Chiang Mai Medical Journal 2018;57(3):151-7.**

Keywords: hospitalization, COPD, COPD exacerbation, GOLD

Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable, progressive, and common lung disease characterized by persistent airflow limitation which is usually caused by an enhanced chronic inflammatory response to noxious particles or gases in the airway and the lungs (1-3). It is the world's sixth leading cause of death (approximately three million in 2012) and is projected to become the third leading cause by 2030 (1). This disease re-

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sults in a serious social and economic burden (2). COPD has been the sixth leading cause of death in Thailand since 2010, after cancer, ischemic heart disease, stroke, lower respiratory infections, and HIV, in that order (4).

Acute exacerbations of COPD (AECOPD) significantly increase mortality in hospitalized COPD patients (3). AECOPD is defined as an acute deterioration of respiratory symptoms that leads to significant consequences for patients such as respiratory failure, increased risk of intubation, infections such as pneumonia, and hospitalization. A history of AECOPD is the most consistent predictor of future AECOPD and is associated with a poor prognosis and increased risk of hospitalization (1,5). In addition, COPD often occurs with other comorbidities that may influence the prognosis, e.g., cardiovascular, gastrointestinal, or metabolic diseases (1,6-10) which can induce exacerbation and lead to hospitalization and death (2).

Apart from pneumonia, chronic kidney disease (CKD), and thalassemia, AECOPD has remained one of the most frequent diagnoses among hospitalized patients at Sarapee Hospital. AECOPD rose from the tenth to the third cause of death in hospitalized patients at Sarapee Hospital in 2015 and 2016, after pneumonia and septicemia. However, there have been no previous official reports of the prevalence of COPD in this hospital. Preventing hospitalization from AECOPD can improve both the mental and physical health of the patient while also benefitting the hospital economically (2,11). This study was designed to determine the prevalence of hospitalization in AECOPD patients as well as to identify factors associated with the severity of the disease and co-morbidities. The findings of this study could potentially help develop management strategies to reduce the hospitalization rate of AECOPD patients.

Methods

Design and participants

This retrospective study included 277 patients diagnosed with AECOPD who had been treated at Sarapee Hospital between October 2015 and September 2016. Only patients whose diagnosis had been confirmed by clinical presentations according to the GOLD guidelines, including the pulmonary function test (PFT) or spirometry, were included. COPD is defined as a post-bronchodilator ratio of forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) < 0.7. Patients with a post-bronchodilator forced expiratory volume in one second-forced vital capacity ratio (FEV1/FEC) less than 0.7 were identified for further analysis (1). We categorized the severity of COPD by using the most recent PFT result of each patient. Prior to analysis, patient records and information were de-identified.

Data sources and variables

Clinically relevant data was collected from the patients' medical records including age, gender, body mass index (BMI), duration of diagnosis, current COPD medication, home oxygen use, severity of COPD categorized by latest recorded GOLD grades (1), current smoking status, and co-morbidities.

Current COPD medication included bronchodilator inhalers, inhaled corticosteroids (ICS), and systemic steroids (SS). Proper use of inhaler was also recorded, evaluated, and scored by a pharmacist using the metered-dose inhaler (MDI) evaluation chart developed by Sarapee Hospital which categorizes the patients as either effective or ineffective users. The most recent score recorded prior to admission was used in the analysis.

We retrieved diagnoses of selected co-morbidities occurring before the date of AECOPD, i.e., ischemic heart disease (IHD), heart failure, atrial fibrillation, gastroesophageal reflux, hypertension, diabetes mellitus, lung cancer, and depression.

The outcome of interest was hospitalization. We categorized the patients into non-hospitalized and ever-hospitalized groups. For patients who had visited the hospital more than one time during the study period, we used the data from the most severe visit as determined by hospitalization, intubation, and length of stay.

Statistical analysis

We used STATA version 12.1 (StataCorp, College Station, TX, USA) for data analysis. Categorical and discrete variables are shown as a percentage; continuous variables are shown as mean and standard deviation (SD). Categorical variables were analyzed using chi-square or Fisher's exact test. Continuous variables were compared using Student's t-test.

Potentially associated factors with *p*-values less than 0.05 were analyzed using binary logistic regression. Results are shown as adjusted odds ratios (aORs) with 95% confidence interval (CI). *p*-values <0.05 are considered as statistically significant.

Results

Of the total 277 AECOPD patients, 150 were females (54.16%). The overall mean age was 72.59 years (SD.=9.60). The average duration of diagnosis was 5.72 years (SD.= 3.17). Among the AECOPD patients, 21.3% were admitted to the hospital at least one time over a 12 month period. Six and a half percent were current smokers and 14% had home oxygen therapy.

All patients had been prescribed bronchodilators, 76.53% had additional inhaled corticosteroids, and 1.45% had oral form of systemic steroids. Severity of the disease categorized by GOLD stages were stage 1-115 cases (41.52%), stage 2-12 cases (4.33%), stage 3-1 case (0.36%), and stage 4-149 cases (53.79%). The most common comorbidity was hypertension, which affected about half of the patients.

Hospitalization of AECOPD patients was significantly associated with higher COPD severity (*p*-value 0.035), inhaled corticosteroid use (*p*-value 0.004), systemic steroids use (*p*-value <0.001), home oxygen use (*p*-value <0.001), and IHD (*p*-value 0.009). Gender, age, BMI, duration of disease, and co-morbidities other than IHD were not significantly associated with hospitalization (Tables 1 and 2).

Regression analysis showed that home oxygen use was statistically significantly associated with higher rates of hospitalization due to AECOPD (aOR = 21.61, 95% CI=8.92 - 52.38, *p*-value <0.001). AECOPD patients with IHD also had a higher rate of hospitalization, but the correlation was not statistically significant (aOR=2.59, 95% CI = 0.89-7.51, *p*-value 0.078) (Table 3).

Discussion

Our study showed that the prevalence of hospitalization in Sarapee Hospital for patients with AECOPD was 21.30% of the total 277 AECOPD cases. The severity of the disease

Table 1. Baseline Sociodemographics of Patients

Data	Hospital Admission(s) in One Year				*p-value*
	None		1		
	n=218	Column %	n=59	Column %	
Gender					
• Female	116	53.21	34	57.63	0.548
• Male	102	46.79	25	42.37	
Mean age, years (SD.)	72.42 (9.26)		73.19 (10.84)		0.591
Body mass index (BMI)					
• Underweight (<18.5)	110	50.46	32	54.24	0.779
• Normal (18.5-24.9)	92	42.20	24	40.68	
• Overweight/obese (≥25)	16	7.34	3	5.08	
Duration of diagnosis, mean (SD)	5.86 (3.69)		5.17 (3.78)		0.218
Smoking					
• Never smoked	204	93.58	53	92.98[+]	0.872
• Current smoker	14	6.42	4	7.02[+]	
Missing	0		2		
Co-morbidities					
• Ischemic heart disease	16	7.34	11	18.64	0.009
• Heart failure	12	5.50	5	8.47	0.401
• Atrial fibrillation	7	3.21	3	5.08	0.496
• Gastroesophageal reflux	5	2.29	4	6.78	0.085
• Hypertension	114	52.59	27	45.76	0.375
• Diabetes mellitus	14	6.42	7	11.86	0.162
• Lung cancer	2	0.92	2	3.39	0.159
• Depression	2	0.92	2	3.39	0.159

[+]; percentage calculated by excluding missing data

Table 2. Severity and treatment

Data	Hospital admission(s) in one year				*p*-value
	None		1		
	n=218	Column %	n=59	Column %	
GOLD stage (latest FEV1)					
• 1 (≥80%)	98	44.95	17	28.81	0.035
• 2 (≤ 50-79.9%)	10	4.59	2	3.39	
• 3 (≤30-49.9%)	1	0.46	0	0	
• 4 (<30%)	109	50	40	67.80	
Current COPD medications					
• Inhaled corticosteroid					
- No	58	26.61	5	8.77+	0.004
- Yes	160	73.39	52	91.23+	
- Missing	0		2		
• Systemic steroids					
- No	218	100	53	92.98+	< 0.001
- Yes	0	0	4	7.02+	
- Missing	0		2		
Proper use of inhaler					
• No	75	34.40	25	43.86+	0.186
• Yes	143	65.60	32	56.14+	
• Missing	0		2		
Home oxygen use					
• No	209	95.87	27	47.37+	< 0.001
• Yes	9	4.13	30	52.63+	
• Missing	0		2		

+; percentage calculated by excluded missing data

Table 3. Relationship Between Hospitalized AECOPD and Associated Factors Analyzed by Multivariate Logistic Regression

	Adjusted OR	95% confidence interval	*p*-value
Inhaled corticosteroid	2.37	0.75-7.47	0.141
Home oxygen use	21.61	8.92-52.38	<0.001
GOLD stage	1.05	0.65-1.68	0.854
Ischemic heart disease	2.59	0.89-7.51	0.078

was positively associated with hospitalization. Home oxygen therapy was the strongest predictor of hospitalization, while co-morbidities, with the exception of IHD, had no statistically significant association.

Regarding to the prevalence of 21.30% in our study, it is slightly higher than found in one prior study. The study shows the hospitalization rate among COPD patients is around 19% (12). However, it is a population-base household survey so the prevalence could be lower than found in our study which the disease of patient tended to be more severe. Another study at Rajavithi Hospital, Bangkok, Thailand found that 50% of AECOPD patients were hospitalized (13). This is more than twice of the founding in our study. This difference could be due to differences in baseline characteristics of the patients including gender and disease severity.

Severity of disease was found to be associated with hospitalization in our study. Those using inhaled corticosteroids, home oxygen, and those with higher GOLD grades (lower FEV1) are potential indicators of COPD severity which are related to hospitalization. However,

when analyzed together, we found that the only statistically significant predictor was home oxygen use. Even we adjusted the severity of the disease in our analysis, this association was still strong.

Oxygen therapy is generally indicated for severely hypoxemic COPD patients or for those with signs of congestive heart failure (1,14). Long-term oxygen therapy (more than 15 hours per day) can reduce the intensity of dyspnea, increase systemic oxygen delivery, and improve respiratory muscle function (15). With this therapy, better outcomes and fewer hospitalizations could be expected. However, we found that the home oxygen use was significantly related to a higher number of hospitalizations in AECOPD patients. This could result from inappropriate use of home oxygen such as inappropriate oxygen concentration or duration of use. As in practice, we sometimes found that when the families perceive that the patient are breathlessness, they think that home oxygen could help. So they give it to the patient without prescription from physicians. Another potential explanation is that high concentrations of oxygen can cause hyperoxemia and/or hypercapnia, conditions that can result in AECOPD, respiratory failure, and hospitalization (11,15). These issues should be explored further.

In the past few years, studies have reported that COPD patients with ischemic heart disease have a higher risk of AECOPD and hospitalization compared to patients with only COPD (16). This is similar to our study that COPD patients with ischemic heart disease trended to have an increased risk of hospitalization. The mechanisms are assumed to be many different biological processes such as hypoxia, systemic inflammation, endothelial dysfunction, heightened platelet reactivity, arterial stiffness, and right ventricle modification. Comorbid IHD is associated with worse health status, lower exercise capacity, and more dyspnea in stable COPD patients as well as with longer exacerbations (17).

Since this was a retrospective cross-sectional study, there were some limitations. Firstly, the study was conducted in a single hospital so the risks identified in this study might not be generalizable to other hospitals. Secondly, there could be other potential risk factors that were not explored in this study, e.g., air pollution, weather, and daily physical activity level. Finally, FEV1 data and MDI evaluations collected in the study were the latest in the medical records but might not represent the current values because no annual evaluation was done.

In conclusion, as severity was found to be associated with hospitalization of AECOPD patients, more action is needed to control the disease and to prevent it from becoming more severe. Moreover, co-morbidities should also be a concerned. Preventing and controlling other diseases should reduce the rate of hospitalization, especially in individuals with a high risk of cardiovascular disease. Providing more education about the disease and proper use of home oxygen could potentially be an important primary factor in reducing the rate of hospitalization for AECOPD.

Ethics

The study was approved by the Ethics Committee from Chiang Mai University (No. 120/2560).

Conflict of Interest

None to declare

References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for diagnosis, management, and prevention of COPD. http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html. Date last updated: February 2013. Date last accessed: July 12 2012.
2. Santibanez M, Garrastazu R, Ruiz-Nunez M, Helguera JM, Arenal S, Bonnardeux C, et al. Predictors of Hospitalized Exacerbations and Mortality in Chronic Obstructive Pulmonary Disease. PloS One. 2016;11:e0158727.
3. Sharafkhaneh A, Spiegelman AM, Main K, Tavakoli-Tabasi S, Lan C, Musher D. Mortality in Patients Admitted for Concurrent COPD Exacerbation and Pneumonia. COPD. 2017;14:23-9.

4. Prevention CCoDCa. Top 10 Causes of Death 2016. [Available from: https://www.cdc.gov/global-health/countries/thailand/default.htm.
5. Margüello MS, Garrastazu R, Ruiz-Nuñez M, Helguera JM, Arenal S, Bonnardeux C, et al. Independent effect of prior exacerbation frequency and disease severity on the risk of future exacerbations of COPD: a retrospective cohort study. NPJ Prim Care Respir Med. 2016;26:16046.
6. Sakae TM, Pizzichini MM, Teixeira PJ, Silva RM, Trevisol DJ, Pizzichini E. Exacerbations of COPD and symptoms of gastroesophageal reflux: a systematic review and meta-analysis. J Bras Pneumol. 2013;39:259-71.
7. Kim J, Lee JH, Kim Y, Kim K, Oh Y-M, Yoo KH, et al. Association between chronic obstructive pulmonary disease and gastroesophageal reflux disease: a national cross-sectional cohort study. BMC Pulm Med. 2013;13:51.
8. Lambert AA, Putcha N, Drummond MB, Boriek AM, Hanania NA, Kim V, et al. Obesity is Associated with Increased Morbidity in Moderate to Severe COPD. Chest. 2017;151:68-77.
9. Bhatt SP, Nanda S, Kintzer JS. Arrhythmias as trigger for acute exacerbations of chronic obstructive pulmonary disease. Resp Med. 2012;106:1134-8.
10. Terada K, Muro S, Sato S, Ohara T, Haruna A, Marumo S, et al. Impact of gastro-oesophageal reflux disease symptoms on COPD exacerbation. Thorax. 2008;63:951-5.
11. Qureshi H, Sharafkhaneh A, Hanania NA. Chronic obstructive pulmonary disease exacerbations: latest evidence and clinical implications. Ther Adv Chronic Dis. 2014;5:212-27.
12. Lim S, Lam DC, Muttalif AR, Yunus F, Wongtim S, Lan le TT, et al. Impact of chronic obstructive pulmonary disease (COPD) in the Asia-Pacific region: the EPIC Asia population-based survey. Asia Pac Fam Med. 2015;14:4.
13. Wiwatcharagoses K, Lueweeravong K. Factors Associated with Hospitalization of Chronic Obstructive Pulmonary Disease Patients with Acute Exacerbation in the Emergency Department, Rajavithi Hospital. J Med Assoc Thai. 2016;99 Suppl 2:S161-7.
14. Katsenos S, Constantopoulos SH. “Long-Term Oxygen Therapy in COPD: Factors Affecting and Ways of Improving Patient Compliance. Pulm Med. 2011;2011:325362. doi: 10.1155/2011/325362. Epub 2011 Sep 15
15. Brill SE, Wedzicha JA. Oxygen therapy in acute exacerbations of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2014; 9:1241-52.
16. Campo G, Pavasini R, Malagu M, Mascetti S, Biscaglia S, Ceconi C, et al. Chronic obstructive pulmonary disease and ischemic heart disease comorbidity: overview of mechanisms and clinical management. Cardiovas Drugs Ther. 2015;29: 147-57.
17. Man JP, Sin DD, Ignaszewski A, Man SFP. The Complex Relationship Between Ischemic Heart Disease and COPD Exacerbations. Chest. 2012; 141:837-8.

การนอนโรงพยาบาลในผู้ป่วยที่มีอาการเฉียบพลันจากโรคปอดอุดกั้นเรื้อรังในโรงพยาบาลสารภี: การศึกษาย้อนหลังหาความชุกและปัจจัยที่เกี่ยวข้อง

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วัตถุประสงค์ เพื่อหาความชุกของการนอนโรงพยาบาลในผู้ป่วยปอดอุดกั้นเรื้อรังที่มีอาการเฉียบพลัน (AECOPD) และความสัมพันธ์กับความรุนแรงของโรค โรคร่วม และการรักษา

วิธีการศึกษา ผู้ป่วย AECOPD ที่ได้รับการวินิจฉัยและรักษาที่โรงพยาบาลสารภี ระหว่างตุลาคม 2558 – กันยายน 2559 ถูกคัดเข้าสู่การศึกษาย้อนหลังนี้จำนวน 277 ราย โดยวัดผลลัพธ์หลักคือการนอนโรงพยาบาลจากอาการเฉียบพลันในโรคปอดอุดกั้นเรื้อรัง

ผลการศึกษา ความชุกในการนอนโรงพยาบาลของผู้ป่วย AECOPD ที่โรงพยาบาลสารภีคือ ร้อยละ 21.3 ปัจจัยที่บ่งบอกความรุนแรงของโรคเป็นตัวทำนายการนอนโรงพยาบาลได้ ซึ่งได้แก่ GOLD grade การใช้ยาสเตียรอยด์และการใช้ออกซิเจนที่บ้าน โดยการใช้ออกซิเจนที่บ้านมีผลมากกว่าปัจจัยอื่น (aOR=21.61, 95% CI = 8.92- 52.38, $p < 0.001$) ยังไม่พบความสัมพันธ์กับการมีโรคร่วม ยกเว้นโรคหัวใจขาดเลือดที่อาจมีแนวโน้มจะพบการนอนโรงพยาบาลมากกว่าโรคอื่น (aOR=2.59, 95% CI=0.89 - 7.51, *p*-value 0.078)

สรุปผลการศึกษา การนอนโรงพยาบาลในผู้ป่วย AECOPD สัมพันธ์กับการใช้ออกซิเจนที่บ้าน และมีแนวโน้มจะเกี่ยวข้องกับโรคหัวใจขาดเลือด การเฝ้าระวังควบคุมโรคไม่ให้แย่ลงโดยการรักษาอย่างเหมาะสม รวมถึงการควบคุมโรคร่วมให้ดีอาจช่วยลดการนอนโรงพยาบาลได้ และควรมีการศึกษาต่อไปถึงความถูกต้องเหมาะสมของการใช้ออกซิเจนที่บ้านด้วย **เชียงใหม่เวชสาร 2561;57(3):151-7.**

คำสำคัญ: การนอนโรงพยาบาล โรคปอดอุดกั้น ถุงลมโป่งพอง ปอดอุดกั้นเฉียบพลัน