Original Article

Profile of Risk Factors for Venous Thromboembolism (VTE) in Acute COPD Exacerbations at Kolonel Abundjani Bangko Regional Hospital

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Submitted: May 8th, 2024
Accepted: October 22nd, 2024
Published: October 31st, 2024

Respir Sci. 2024; 5(1): 19-27
https://doi.org/10.36497/respirsci.v5i1.151

Abstract

Background: Acute exacerbation of COPD is characterized by dyspnea and/or cough with worsening sputum production for <14 days. Patients with acute exacerbations of COPD are at increased risk of vascular events, including venous thromboembolism (VTE). VTE risk factor assessment can be carried out using a scoring system to estimate the risk of a patient experiencing VTE before further examination is conducted.

Method: This study used a cross-sectional approach. Research subjects were selected from patients diagnosed with acute exacerbation of COPD at Kolonel Abundjani Bangko Regional Hospital from November 2023 to January 2024. Patient data were extracted from medical records, and then patients who were compatible with the inclusion criteria were interviewed using the Wells and Padua criteria**.** Univariate analysis was conducted to assess the characteristics of VTE risk in acute exacerbation of COPD. Bivariate analysis was utilized to determine the correlation between the exacerbation of COPD and VTE risk using the chi-square test.

Results: A total of 20 cases of acute exacerbation of COPD were identified from November 2023 to January 2024. Based on Wells's criteria, as many as 18 patients (90%) were not at risk of developing VTE. Based on Padua criteria, 13 patients (65%) were at low risk and 7 patients (7%) were at high risk of developing VTE. The most common patient characteristics based on the scoring system are an increase in heart rate >100x according to the Wells criteria and the presence of acute infections or rheumatological disorders, which represent the Padua criteria. There is no correlation between acute exacerbation of COPD and VTE risk scoring.

Conclusion: The majority of patients with acute exacerbation of COPD are not at risk of developing VTE. There is no correlation between acute exacerbation of COPD and the risk of VTE.

Keywords: acute exacerbation of COPD, venous thromboembolism (VTE), Wells criteria, Padua criteria

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality, which increases the economic and social burden quite significantly.[1] Based on data from the World Health Organization (WHO), COPD is the third cause of death, with a total of 3.23 million deaths worldwide in 2019.[2]

Acute exacerbation of COPD (AECOPD) is characterized by dyspnea and/or cough with worsening sputum production for <14 days. These onsets are usually associated with local and systemic inflammation caused by respiratory tract infections, pollution, and other causes that impact the lungs. Based on guidelines from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023, AECOPD is classified based on the degree of severity, which consists of mild, moderate, and severe.[1]

Hospitalized patients with acute exacerbations of COPD are at increased risk of vascular events, including venous thromboembolism (VTE), which is more commonly known as a manifestation of deep vein thrombosis (DVT) and pulmonary embolism (PE).[3]

COPD was assessed as a moderate risk factor for VTE. In previous research, it was found that COPD patients who suffered from VTE had a two-times higher risk of death than those who suffered from VTE without COPD. About 50% of stage III/IV COPD patients die within 3.5 months after the VTE event. Several risk factors for VTE in COPD patients include immobilization, bronchial superinfection, right ventricular failure, and venous outflow stasis.[3,4]

Assessment of VTE risk factors in patients can be carried out using a scoring system, which makes it easier to stratify patients in estimating the patient's risk of developing VTE before further examination is carried out. So far, VTE risk factor scoring has been approved by the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), some of which include Wells criteria and Padua criteria.[5]

Based on a review of the existence of vascular risk factors, especially in patients with AECOPD, as well as the limited research related to this in Indonesia, the researchers were interested in examining the risk profile of VTE events in patients with AECOPD at Kolonel Abundjani Bangko Regional Hospital, which is one of the hospitals in Merangin Regency, Jambi, Indonesia.

METHOD

This was a descriptive observational study with a cross-sectional approach taken from patients diagnosed with AECOPD at the Kolonel Abundjani Bangko Regional Hospital. The research sample included all patients with AECOPD who were admitted to Kolonel Abundjani Regional Hospital from November 2023 to January 2024. Researchers excluded patients with AECOPD who refused to be interviewed.

Patients' data were taken from medical records and those who met the

inclusion criteria were then interviewed using the Wells and Padua criteria. The data and scoring results were recorded and collected using Microsoft Excel and analyzed using Statistical Product and Science Service (SPSS) 26th version. Data analysis and presentation were processed using univariate analysis to assess the characteristics of VTE risk in AECOPD. Bivariate analysis was utilized to determine the correlation between AECOPD and VTE risk using the Chi-Square test.

RESULTS

There were 20 cases of AECOPD during November 2023–January 2024 that met the inclusion and exclusion criteria.

Table 1. Characteristic of AECOPD at Kolonel Abundjani Bangko Regional Hospital (N=20)

Characteristics	N (%)
Gender	
Male	19 (95%)
Female	1 (5%)
Age	
56 – 65 years	11 (55%)
>65 years old	9 (45%)
Smoking History (Brinkman Index)	
Mild smoker	0 (0%)
Moderate smoker	1 (5%)
Heavy smoker	19 (95%)
Modified Medical Research Council Scale	
0	0 (0%)
1	0 (0%)
2	0 (0%)
3	15 (75%)
4	5 (25%)
Classification of Exacerbations (Anthonisen)	
Type I Exacerbation	15 (75%)
Type II Exacerbation	3 (15%)
Type III Exacerbation	2 (10%)

Table 1 shows the characteristics of AECOPD patients at Kolonel Abundjani Regional Hospital. Based on gender, 19 patients (95%) were male and 1 (5%) was female. The age of the patients was predominantly over 55 years, with 11 people (55%) in the range of 56–65 years old and 9 people (45%) in the range >65 years. A total of 19 (95%) AECOPD patients were classified as heavy smokers, and only 1 patient (5%) was classified as a moderate smoker.

Based on the Modified Medical Research Council Scale (mMRC), all respondents (100%) were at mMRC level ≥2. Based on the classification of exacerbations, as many as 15 patients (75%) had type I (severe) exacerbations, 3 patients (15%) had type II (moderate) exacerbations, and 2 patients (10%) had type III (mild) exacerbations. Patients with AECOPD were grouped based on the results of the risk of VTE events using the Wells and Padua criteria.

Table 2. Risk assessment of VTE using Wells score (PE and DVT) (N=20)

Wells Criteria	N (%)
PE	
Unlikely	18 (90%)
Likely	2 (10%)
DVT	
Unlikely	18 (90%)
Likely	2 (10%)

If the results of Wells criteria (PE) >4, then there is a risk of causing PE. Table 2 shows that 18 people (90%) were not at risk of PE, and 2 people (10%) were at risk of PE.

Table 3. VTE risk criteria based on Wells score (PE and DVT)

Wells Criteria	N (%)
PE	
Heart rate >100x/m	11 (55%)
Alternative diagnoses other than PE/DVT are unlikely	0 (0%)
Hemoptysis	0 (0%)
History of cancer	0 (0%)
History of immobilization or surgery	5 (25%)
History of DVT/PE	0 (0%)
Clinical signs and symptoms of DVT (leg edema and pain on palpation of deep vein)	2 (10%)
DVT	
Active cancer	0 (0%)
Paralysis, paresis of lower limbs	0 (0%)
History of bed rest 3 days or major surgery 4 weeks	5 (25%)
Swelling of the entire leg	0 (0%)
Swelling in deep vein distribution area	0 (0%)
Swelling >3 cm compared to asymptomatic leg	2 (10%)
Pitting edema	2 (10%)
History of DVT	0 (0%)
Non-varicose superficial collateral veins	0 (0%)
Alternative diagnosis is at least as likely	0 (0%)

In assessing the risk of DVT, a Wells score of ≥2 is considered to be at risk of causing DVT. About 18 patients (90%) were not at risk of DVT, and 2 patients (10%) were at risk of DVT.

In Table 3, it was found that the risk characteristics of VTE based on Wells score (PE) in patients included: heart rate >100x/minute that was found in 11 patients (55%), immobilization that was observed in 5 patients (25%), and 2 patients with signs and symptoms of DVT (10%).

Characteristics of patients with AECOPD based on Wells score (DVT) are shown in Table 3. A total of 5 patients (25%) had a history of immobilization, 2 patients (10%) had swelling in the legs >3 cm compared to the legs without complaints, and 2 patients (10%) had pitting edema.

Another criterion that can be used for assessing the risk of VTE events is the Padua criteria; if the scoring result is ≥4, the patient is at high risk of developing VTE. Table 4 shows that 13 patients (65%) are at low risk, and 7 patients (35%) are at high risk.

Table 4. Risk assessment of VTE using Padua score (N=20)

Padua Criteria	N (%)
Low risk	13 (65%)
High Risk	7 (35%)

Based on the Padua scoring assessment in Table 5, five patients (25%) had a history of bed rest ≥3 days, 6 patients (30%) had thrombophilia, 8 patients (40%) were over 70 years old,

respiratory/heart failure was found only in 1 patient (5%), acute infections and/or rheumatological disorders in 2 patients, and obesity (BMI ≥30 kg/m^2) was observed in 2 patients (10%).

Table 5. Characteristics of VTE Risk Factor using Padua criteria

Padua Criteria	N (%)
Alternative diagnoses other than PE/DVT are unlikely	0 (0%)
Cancer History	0 (0%)
Bed rest ≥3 days	5 (25%)
Thrombophilia	6 (30%)
Age ≥70 years	8 (40%)
Respiratory/heart failure	1 (5%)
Acute myocardial infarction and/or ischemic stroke	0 (0%)
Acute infection and/or rheumatological disorders	13 (65%)
Obesity (BMI ≥30 kg/m^2)	2 (10%)
Hormonal therapy	0 (0%)

Based on the chi-square test, there is no correlation between AECOPD and the risk of VTE using Wells criteria, with a value of P=0.690. Also note the correlation between AECOPD and the risk of VTE using Padua criteria, there is no correlation with a value of P=0.896 (Tabel 6).

Table 6. Correlation between AECOPD and VTE risk using Wells criteria and Padua criteria (N=20)

Correlation of VTE risk and AECOPD	P
using Wells criteria	0.690*
using Padua criteria	0.896*

Note: *chi-square tests

DISCUSSION

Based on the characteristics of AECOPD patients, there were more male patients (95%) than females (5%). These are following studies conducted by Zhang et al in China, which stated that 64.2% of COPD patients were male, while 35.8% were female.[6]

Even though it is generally considered that COPD disease occurs in older men, the prevalence of COPD continues to increase in women in line with the high smoking rate.[7] Based on data from the Centers for Disease Control and Prevention (CDC) from 2011 to 2020, it was found that in adulthood, the prevalence of COPD in women was higher than in men.[8]

Based on age, the largest age group was the 50–65 years range in 11 patients (55%), while 9 patients (45%) were in the age range >65 years. The prevalence of COPD is two to three times higher at age 60 than at younger ages. As age increases, a progressive decline in lung function is found, including a decrease in FEV_1 of around 20 ml/year, followed by a decrease in FEV_1/FVC and an increase in residual volume with persistent lung capacity. These changes in lung function cause a decrease in oxygen levels and the ability to eliminate CO_2 due to a decrease in compliance lungs and elasticity recoil lungs.[9]

The smoking history of patients with AECOPD was measured based on the Brinkman Index, and it was found that 19 patients (95%) had a history of being heavy smokers. Based on studies conducted by Au, tobacco smoke is a potent stimulant in triggering inflammation and increasing the risk of exacerbations.[10] In line with this research, Dahl et al also noticed that increased concentrations of

CRP, a marker of inflammation, were associated with an increased risk of exacerbations and death in COPD.[11]

Based on evaluation using mMRC, all patients were at mMRC level ≥2. Dyspnea is the most disturbing complaint and causes activity limitations in COPD patients. The mMRC is used to measure degrees of dyspnea that is associated with daily activities. mMRC ≥2 is used as a cut-off for severe symptoms.[12]

In COPD, there are thickening of the bronchial walls and a reduction of elastic fibers, which cause bronchial collapse and increase hyperinflation and dyspnea. Perez explained that there was a significant relationship between the level of exacerbations on the mMRC scale.[13]

Anthonisen described COPD exacerbation as an acute and ongoing disorder that included at least 2 of these symptoms: dyspnea, an increase in sputum volume, and a change in sputum color.[14] Based on this research, it was found that, according to the Anthonisen Classification, the highest degree of exacerbation was type I (75%).

Patients with AECOPD were then interviewed using risk factor scoring using Wells criteria. Based on Wells's criteria, the incidence of PE and DVT each had the same results. About 18 patients (90%) were not at risk, and 2 patients (10%) were at risk of developing PE and DVT. These results are supported by a study conducted by Gunen et al which stated that as many as 16% of COPD exacerbation patients were confirmed to have VTE as a complication or trigger factor after going through screening using the Wells criteria and confirmed via CT angiography examination.[15]

PE can worsen symptoms in COPD patients, although it is very difficult to distinguish it from other causes of exacerbation by clinical criteria. The prevalence of PE in patients with AECOPD ranges from 0 to 29%; this figure cannot be determined with certainty due to the limited number of studies related to this research.[15] DVT has a much lower prevalence in patients with AECOPD, ranging from 1.6 to 12.7%.[16]

Based on the assessment of acute COPD exacerbations using the Padua scoring, more patients (65%) were at low risk than those with high risk (35%) of developing VTE. Based on GOLD 2023, thromboprophylaxis therapy should be given to patients with AECOPD who are hospitalized at high risk.[1]

Furthermore, an analysis of the characteristics of the risk of VTE was carried out in patients with AECOPD. The highest risk of VTE was heart rate >100 times/minute in as many as 11 patients (55%) which represented the Wells (PE), and acute infection and/or rheumatology in as many as 13 patients (65%) representing the Padua criteria.

A study conducted by Warnier et al concluded that increased heart rate was a strong and independent risk factor for all causes of death in patients diagnosed with COPD, but there was no significant relationship between heart rate and other respiratory complications such as exacerbations and pneumonia in COPD

patients. In general, patients with COPD have a higher heart rate than patients without COPD. This is due to the risk of endothelial dysfunction caused by smoking, which triggers autonomic dysfunction due to tissue hypoxemia.[17]

The main cause of AECOPD is infection. Around 40–60% of cases are caused by bacterial infections, 30% are caused by viruses, and 5-10% are caused by atypical bacteria. COPD patients experience disturbances in the lung defense mechanism, as a consequence causing the proliferation of PPB (potentially pathogenic bacteria) and increasing bronchial secretions.[18]

In a retrospective study comparing the effectiveness of VTE risk assessment scoring, it was found that, in general, the Wells score was superior to the Padua score in predicting the risk of developing VTE. Wells's score had modifiable risk factors for VTE events, such as hemoptysis and heart rate that could reflect the status quo of patients when entering treatment, whereas the Padua score did not include this criteria.[5] Based on a cohort study conducted in China, Yang et al concluded that the Padua predictive score might not be appropriate to predict VTE risk in hospitalized patients with acute respiratory conditions.[19]

Although AECOPD increases the risk of vascular events, including VTE, our study shows that there is no correlation between AECOPD and the risk of VTE. Based on a previous study from Sadeghi et al, it was indicated that using Wells criteria based on the patient's condition was not an appropriate diagnostic tool for PE; it is necessary to combine different measurements of D-dimer level to provide a more accurate diagnostic protocol for PE.[20]

Currently, there are few studies on the prevalence of VTE among patients with acute exacerbations of COPD, particularly using VTE risk scoring to investigate. Most studies assessed VTE using suitable examination tools such as D-dimer and CT angiography. Considering the small number of our patients and limited reliable examinations in our hospital, these may affect the results of our study. Hence, further research to improve our limitations is warranted.

CONCLUSION

The characteristics of COPD patients with acute exacerbations at the Kolonel Abundjani Bangko Regional Hospital are dominated by males, age range of 56-65 years, a history of heavy smoking, and admission to the hospital with type I exacerbation. The most common clinical symptoms of VTE are an increase in heart rate >100x/minute and the presence of an acute infection that precedes the onset of an exacerbation in the patient.

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