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A study on the correlation between clinical features, spirometry and ABG in acute exacerbation of obstructive lung diseases

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Abstract

Background: Obstructive lung diseases are those characterized by limitation of expiration of air from lungs, which may occur due to narrowing of airways or damage to the lungs. They include COPD, bronchial asthma, bronchiectasis and cystic fibrosis. These illnesses are punctuated by “exacerbations”, which are acute episodes of worsening of symptoms including cough, breathlessness and increased sputum production. The degree of airflow impairment may be assessed using bedside spirometry, especially the measures of expiratory function like forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and the ratio FEV1/FVC. The impairment in gas exchange resulting from obstructive pathology can be assessed using arterial blood gas analysis (ABG). Our study aims to employ ABG and spirometry to assess the degree of impairment in 50 patients admitted with acute exacerbation of obstructive lung diseases in our tertiary care hospital in rural South India. The present study also aims to identify any correlation between clinical features and values of ABG and spirometry, to assess if FEV1 values can help predict requirement of ABG, if ABG values can predict onset of respiratory failure before overt symptoms appear, and to identify if change in pH levels with pCO₂ can be used as a predictive marker for respiratory failure.

Methods: We studied clinical features and ABG values and spirometry values on admission and on discharge in 50 patients admitted to Rajah Muthiah Medical college between September 2019 – October 2021.

Results: An admission pH of less than 7.20, a pCO₂ of more than 60 and a pO₂ of less than 60 and FEV1 of less than 68% of normal are the major factors associated with respiratory failure.

Conclusions: There is a correlation between FEV1 and pCO₂ [p value 0.09] in determining severity of acute exacerbation of obstructive lung disease. Combining spirometric criteria with clinical criteria increases specificity and overall accuracy in predicting respiratory failure.

Keywords: obstructive lung diseases, acute exacerbation, ABG, spirometry, FEV1

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of mortality and the 12th leading cause of disability worldwide today. Worldwide, COPD has a prevalence of 15% among the elderly. It is currently the 6th most common cause of death worldwide and it is estimated to become an even more common cause of mortality worldwide [3, 4]

The chronic and progressive course of chronic obstructive pulmonary disease (COPD) is often punctuated by “exacerbations”, defined clinically as episodes of increasing respiratory symptoms, particularly dyspnoea, cough and sputum production, and increased sputum purulence. COPD exacerbations have a negative impact on the quality of life of patients with COPD, accelerate disease progression, and can result in hospital admissions and death [1]. Mortality rate of 20.3% have been identified in studies among patients with acute exacerbations.

COPD and its acute exacerbations are characterized by limitation of expiratory airflow. This can be measured by bedside spirometry. Also used in the evaluation of COPD patients in acute distress are chest radiography, sputum examination, arterial blood gas (ABG) analysis and investigations to identify triggering factors. Arterial blood gas analysis identifies the impaired gas exchange that occurs in an acute exacerbation. This study aims to utilize ABG and spirometric readings, which are measures of the degree of physiological impairment in acute exacerbations of COPD, to identify possible correlation with clinical course and

outcome of the patient. The study also aims to identify if said ABG and spirometric readings can help predict onset of respiratory failure in these patients and the need for ventilatory support.

Materials and Methods

Study Design: Prospective observational study.

Study Duration: September 2019 to October 2021.

Study Sample: 50 cases admitted in Department of Medicine in RMMCH with acute exacerbation of obstructive lung diseases.

Inclusion Criteria

All patients with exacerbation of obstructive lung disease in the age group of 18-85 years

Exclusion Criteria

1. Patients aged less than 18 and more than 85 years
2. Patients with stable obstructive lung disease
3. Patients with restrictive lung disease or tuberculosis
4. Patients with Covid-19.

Methodology

The study was conducted among 50 patients admitted with acute exacerbation of obstructive lung disease in the Department of Medicine of Rajah Muthiah Medical College Hospital during the study period from September 2019 to October 2021. Those patients meeting the inclusion criteria were recruited for the study. Approval from the Institutional Human Ethics Committee was obtained prior to the study. After obtaining informed written consent from the patients or their attendant, detailed history relating to the respiratory illness, symptoms, past history and comorbid illnesses were obtained. Clinical examination of the patient was done. The history along with examination findings were entered in the case proforma.

ABG and spirometry readings were obtained at admission and at discharge and values were entered in case proforma. Results of other routine investigations done were also obtained from the patient case sheets.

Laboratory Methods

An arterial blood sample was drawn at admission and sent for Arterial Blood Gas analysis for each patient. These samples were processed for ABG using radiometer ab180 flex ABG machine. Spirometry was performed for each patient bedside using contec sp10bt handheld spirometer. The patients' treatment, clinical progression, development of complications and treatment outcome were followed up. ABG analysis and spirometry were repeated just prior to discharge of the patient from the hospital. Chest X-ray, sputum analysis and CT chest findings were also considered for analysis.

Results

Gender Distribution

Table 1: Gender distribution

Gender	Percentage
Male	72
Female	28
Total	100

Gender distribution shows males constitute 72% and females represent

Age Distribution

Age distribution shows that 61 to 70 is the most common followed by 51 to 60. The mean age of the study patients is 53 YEARS

Table 2: Age Distribution

Age	Mild	Moderate	Total	Percentage
71 to 80 years	0	3	3	6
61 to 70 years	9	6	15	30
51 to 60 years	9	5	14	28
41 to 50 years	6	2	8	16
21 to 30 years	2	4	6	12
31 to 40 years	2	2	4	8

Table 3: COPD Severity (Gold Criteria)

	Mild/ stage I	Moderate/ stage II	Sever/ stage III	Very severe/ stage IV
Male	20	16	0	0
Female	8	6	0	0
Total	28	22	0	0

Occupation

Occupation distribution shows that the most common occupation pursued by the patients is farming followed by house wife

Place of Residence

Residence distribution shows that most patients are natives of Chidambaram followed by Bhuvanagiri

Smoking

Data represented shows that smoking is a major risk factor with 46% (23) patients of mild disease and 36% (18) patients of moderate disease being smokers

Table 4: BMI

Vitals					
	N	Minimum	Maximum	Mean	Std. Deviation
Height	50	151	170	161.60	5.010
Weight	50	46	80	61.90	9.410
BMI	50	17.60	32.80	23.8718	3.87887

Table shows that the mean BMI was 23.8 with a standard deviation of 3.8

Table 5: Clinical Features

Clinical features	N	Y
Exertional dyspnea	48	2
Cough	4	46
Increased sputum production	3	47
Wheeze	0	50
Decreased exercise tolerance	0	50
Fatigue	42	8
Fever	47	3
Hemoptysis	50	0
Acute onset	0	50

Table shows that wheeze and decreased exercise tolerance are the most common symptoms in acute exacerbation followed by cough and increased sputum production with hemoptysis, exertional dyspnea and fever being the least common.

Table 6: Gold criteria ^[1] classification of COPD on admission

Characteristics		Mild	Moderate	Total (n)	Percentage (%)	P value
Exertional dyspnea	N	27	21	48	96	0.691
	Y	1	1	2	4	
Decreased exercise tolerance		28	22	50	100	
Wheeze		28	22	50	100	
Chronic cough	N	2	2	4	8	0.598
	Y	26	20	46	92	
Fatigue	N	23	19	42	84	0.498
	Y	5	3	8	16	
Fever	N	27	20	47	94	0.409
	Y	1	2	3	6	
Smoking	N	23	18	41	82	0.629
	Y	5	4	9	18	
Cad	N	26	21	47	94	0.591
	Y	2	1	3	6	
Htn	N	25	21	46	92	0.402
	Y	3	1	4	8	
Dm	N	23	21	44	88	0.160
	Y	5	1	6	12	

Table 7: Clinical Findings

Characteristics		Frequency (n)	Percentage (%)
Anemia	Yes	19	38
	No	31	62
Icterus	Yes	0	0
	No	50	100
Cyanosis	Yes	1	2
	No	49	98
Clubbing	Yes	0	0
	No	50	100
Lymphadenopathy	Yes	0	0
	No	50	100
Edema	Yes	1	2
	No	49	98
Raised JVP	Yes	2	4
	No	48	96
Respiratory system	NVBS	2	4
	Wheeze	44	88
	Wheeze + coarse crepts in left lower zone	1	2
	Wheeze + coarse crepts in right lower zone	2	4
	Wheeze, fine bilateral basal crepts	1	2
	S1S2+	48	96
Cardiovascular system	S1S2+, S3 gallop	2	4

ABG and spirometry on admission**Table 8:** Association of ABG on admission with respiratory failure

ABG	Respiratory Failure	N	Mean	Std. Deviation	95% Confidence Interval		T test	P value
					Lower	Upper		
Ph	Yes	10	7.1290	.08698	-1.12368	.00218	-1.941	.058
	No	40	7.1898	.08888				
pO ₂	Yes	10	91.50	8.489	-4.153	8.253	.729	.482
	No	40	89.45	5.311				
pCO ₂	Yes	10	58.60	5.358	2.500	8.300	3.744	.000
	No	40	53.20	3.722				
HCO ₃	Yes	10	15.80	.919	-1.183	.833	-.349	.729
	No	40	15.98	1.510				

Table shows that the mean pCO₂ in patients with respiratory failure was 58.6 whereas in other patients it was 53.2. On analysis of correlation between ABG at admission and

incidence of respiratory failure only pCO₂ showed significant association.

Table 9: Association of Spirometry on admission with respiratory failure

Spirometry	Respiratory Failure	N	Mean	Std. Deviation	95% Confidence Interval		T test	P value
					Lower	Upper		
FEV1	Yes	10	68.10	8.439	-5.781	5.931	.026	.980
	No	40	68.03	8.192				
FVC	Yes	10	81.20	5.287	-4.631	3.581	-.257	.798
	No	40	81.73	5.883				
FEV1/FVC	Yes	10	83.60	10.885	-6.689	7.839	.159	.874
	No	40	83.03	10.057				

Table shows that the mean FEV1 in patients was 68% and mean FVC was 81% and mean FEV1/FVC was 83. On analysis of correlation between spirometry at admission and

incidence of respiratory failure no significant association was found [2].

Correlation between ABG and spirometry on admission

Table 10: Samples Correlations between ABG and Spirometry at admission

	N	Correlation	Sig.
pCO2 admission & FEV1 admission	50	-.038	.791
pCO2 admission & FVC admission	50	-.157	.277
Pco2 admission & FEV1/FVC admission	50	.043	.766
po2admission & fev1admission	50	.050	.733
pO2 admission & FVC admission	50	-.078	.591
pO2 admission & FEV1/FVC admission	50	.107	.458
Ph admission & FEV1 admission	50	-.059	.684
Ph admission & FVC admission	50	-.253	.076
Ph admission & FEV1/FVC admission	50	.088	.544
HCO3 admission & FEV1 admission	50	-.108	.454
HCO3 admission & FVC admission	50	-.104	.471
HCO3 admission & FEV1/FVC admission	50	-.058	.688

Table shows that there is no significant correlation between spirometry and ABG at admission

Table 11: Outcome

Respiratory failure	Yes	10	20
	No	40	80
Ventilatory support	Yes	6	12
	No	44	88
Death	Yes	0	0
	No	100	100

Discussion

GENDER- Out of 50 patients in the study population, 14 (28%) were female. This is much less compared to the data from the western population. The percentage of female patients in the studies by Steer *et al* [27] involving western population ranges from 42-53%. This could be because of the decreased prevalence of smoking among the Indian women. Another reason is reduced presentation of illness to medical care is common among Indian women. The risk factors for developing COPD by women are passive smoking, indoor air pollution and biomass fuel. The incidence of COPD in the women population is increasing worldwide.

AGE- The average of patients in our study was 53 whereas Emerman *et al* found that the average of patients was 64 years in their study.

BMI- The mean BMI was 23.8. Since most of the participants are middle aged working group they were in BMI range of normal to overweight 89.64% (n=140). There is no correlation of BMI with severity of obstructive pattern in our study.

Smoking -The study showed that there is an increased association of COPD with smoking which is consistent with other studies. Smoking in any form found has been regarded as the most important risk factor in almost every study for

developing the disease and has been proven to have a dose – response relationship. On reviewing several studies on male Indian COPD patients, 83.2% were associated with smoking [3].

Occupation - The most common occupation in our study group was farming. Farmers are constantly exposed to dust, minerals and noxious chemicals and the risk is further compounded if smoking is also present. [4]

Symptoms-In our study, most of the patients had chronic cough with wheezing [92%] followed by decreased exercise tolerance and sputum production

CXR- Consolidation, as detected by the chest x-ray, was found to be present in 3(6%) among the study population. The prevalence of consolidation in our study was similar was less than the prevalence seen in Lieberman D *et al* [28] at 29% It indicated the most of the acute exacerbation of COPD were related to weather changes and increased smoking in winter season.

Sanders *et al* [5] report emphysematous changes in 50-80 % of patients with acute exacerbation of COPD which is consistent with our study 88%

Spirometry - The FEV1/ FVC ratio also one of the criteria for defining COPD. Swanney *et al* (2008) [6] documented the importance of this ratio in their study. In our study the FEV1/ FVC ratio ranges from 0.5 – 0.69. Thus statistically

proving that there is a relation between FEV1/ FVC ratio and severity of COPD. The initial ABG showed average pH of 7.43 and average pCO₂ of more than 45 with pO₂ of less than 60 on admission FVC was 53% and FEV1 was 38%.

There was no correlation between initial pO₂ and FEV1. there was moderate correlation between pCO₂ and FEV1 according to Emerman *et al* [8] and gupta *et al*.

Whereas palmer *et al* and miyamoto *et al* found a correlation between FEV1 and pCO₂ in COPD. Our study findings conform to the findings of Emerman *et al* as it shows there was no correlation between pO₂ and FEV1 and only mild correlation between pCO₂ and FEV1

Murray *et al* [7] found that pCO₂ of more than 45 and pO₂ of less than 50 was associated with respiratory failure. This is line with our study where all patients with respiratory failure had pCO₂ of more than 45.

Emerman *et al* conclude that pCO₂ would not increase till FEV1 falls to 35%. Emerman *et al*. also state that 31% of the patients in their study with FEV1 less than 40% of predicted went into respiratory failure.

They also conclude that ABG is a poor predictor of severity of airflow limitation and out come and should be combined with spirometry and other clinical features

According to them the Criteria for admission is FEV1 less than 40% and pO₂ less than 60% and pCO₂ more than 45%. Their findings for pCO₂ correlate well with our study [58%] whereas the findings for FEV1 are in contrast to theirs with all admitted patients having an average FEV1 of 68%. ABG- Khilnani *et al* [9] have found pH <7.26 to be significant with respect to need for mechanical ventilation. Hoo *et al* [10] have also identified pH <7.25 to be significant, with maximum rate of intubation with pH <7.20. Kumar *et al* have found pH <7.20 to be a significant predictor. In our study, a similar trend was found patients with pH <7.2 on the first day eventually having gone for mechanical ventilation. Ventilation-perfusion mismatch, alveolar hypoventilation and respiratory muscle fatigue are reasons for acidosis in severe acute exacerbations.

pCO₂ >68 mm Hg has been described by Kumar *et al* [11] as a significant predictor of mechanical ventilation. In our study, first day pCO₂ > 60 mm Hg has been found to be significant as 80% of patients with pCO₂ > 60 mm Hg needed mechanical ventilation during the course of their hospital stay. Ventilation perfusion mismatch, alveolar hypoventilation and respiratory muscle fatigue are reasons for increased pCO₂ in severe acute exacerbations.

“Culture- Gompertz S, *et al* [12] isolated *Streptococcus pneumoniae*. *H. influenza* was the most commonest with 45% in a study on acute exacerbation in COPD. Similar study by Anja Ede *et al* [13] shows that *Streptococcus pneumoniae*, non typable *H. influenza* and to some extent *Moraxella* are responsible for acute exacerbation in COPD. In contrast to western literature Indian studies by Madhavi *et al* [14]. review shows no isolates of *H. influenza* in acute exacerbation of COPD patients. “*Staphylococcus aureus*, and *Streptococcus pyogenes* were most common gram positive organisms causing acute exacerbation of COPD. In our study of 50 patients, in sputum culture *Klebsiella pneumoniae* was grown in 6 % patients. Next to *Klebsiella pneumoniae*, *Pneumococcus* and *Staphylococcus* was the second most common organism grown in culture. In contrast to other studies where Gram positive organisms like *Streptococcus pneumoniae*, *H. influenza* and *Moraxella* are responsible for Acute exacerbation of COPD. Our study

shows the most common organism responsible for acute exacerbation of COPD is predominantly Gram negative *Klebsiella* [15].

Conclusion

- Increasing age is associated with increased severity of acute exacerbation of obstructive lung disease [16].
- Males are more commonly affected than females [17].
- Smoking is the most common risk factor associated with obstructive lung diseases [18].
- Occupational exposure to risk factors compounds the risk of developing the disease [19].
- The average BMI of patients is 24. This correlates with the study by Camargo *et al* [20].
- We can conclude that elevated pCO₂ and decreased pO₂ and decreased FEV1 on admission is associated with increased incidence of respiratory failure [21].
- Patients with pH in the range of 7.11 to 7.20 were prone to develop respiratory failure [22].
- A pCO₂ of more than 60 and pO₂ of less than 60 is a major factor associated with respiratory failure as evidenced by the study [23].
- Patients with FEV1 less than 68% of normal are at an increased risk of respiratory failure [24].
- There is no correlation between FEV1 and pO₂ [25] in determining severity of acute exacerbation of obstructive lung disease. [Correlates with Gupta *et al*]
- There is a weak correlation between FEV1 and pCO₂ [26] in determining severity of acute exacerbation of obstructive lung disease. [Correlates with Palmer *et al*]
- ABG is indicated at FEV1 less than 68 % of predicted in patients of acute exacerbation of obstructive lung disease to predict impending respiratory failure, the value being arrived at from cases assessed in the study [27].
- Combining spirometric criteria with clinical criteria increases specificity and overall accuracy in predicting respiratory failure. [28] We conclude that patients with a post treatment FEV1 of 40 percent or greater of predicted normal and pCO₂ less than 45 may be discharged [30].
- We found no significant difference of post treatment pO₂, pCO₂, or pH between the patients who were successfully discharged without complications and those that were discharged after respiratory failure [31].
- *Klebsiella* is the most common organism grown in sputum culture of patients with acute exacerbation of COPD in an In-patient setting at a tertiary care hospital [29].

References

1. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease GOLD Executive Summary Jørgen Vestbo 1, 2, Suzanne S. Hurd 3, Alvar G. Agustí 4, Paul W. Jones 5, Claus Vogelmeier 6, Antonio Anzueto 7, Peter J. Barnes 8, Leonardo M. Fabbri 9, Fernando J. Martinez 10, Masaharu Nishimura 11, Robert A. Stockley 12, Don D. Sin 13, and Roberto Rodriguez-Roisin 4. Am J Respir Crit Care Med Vol 187, Iss. 4, pp 347–365, Feb 15, 2013. Copyright © 2013 by the American Thoracic Society Originally Published in

- Press as DOI: 10.1164/rccm.201204-0596PP on August 9, 2012
2. National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma (EPR-3). 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/index.htm>. Accessed July 16, 2015.
 3. Buist AS, Mc Burnie MA, Vollmer WM, *et al.* International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet*. 2007;370:741-750.
 4. Vollmer WM, Gislason T, Burney P, *et al.* Comparison of spirometry criteria for the diagnosis of COPD: results from the BOLD study. *Eur Respir J*. 2009;34:588-597
 5. Aggarwal AN, Chaudhry K, Chhabra SK, D Souza GA, Gupta D, Jindal SK, Katiyar SK, Kumar R, Shah B, Vijayan VK. Prevalence and risk factors for bronchial asthma in Indian adults: a multicentre study. *Indian Journal of Chest Diseases and Allied Sciences*. 2006 Jan 18;48(1):13.
 6. Svanes C, Sunyer J, Plana E, *et al.* Early life origins of chronic obstructive pulmonary disease. *Thorax* 2009; [Epub ahead of print DOI: 10.1136/thx.2008.112136]
 7. Moffatt MF, Kabesch M, Liang L, *et al.* Genetic variants regulating ORMDL3 expression contribute to the risk of childhood asthma. *Nature*. 2007;448:470-3
 8. Bunyavanich S, Schadt EE. Systems biology of asthma and allergic diseases: A multiscale approach. *J Allergy Clin Immunol*. 2015;135:31-42
 9. Tsang KW, Lam SK, Lam WK, *et al.* High seroprevalence of *Helicobacter pylori* in active bronchiectasis. *Am J Respir Crit Care Med*. 1998 Oct. 158(4):1047-51.
 10. Gadek JE, Fells GA, Crystal RG. Cigarette smoking induces functional antiprotease deficiency in the lower respiratory tract of humans. *Science*. 1979;206:1315-1316.
 11. National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma (EPR-3). 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/index.htm>. Accessed July 16, 2015.
 12. Papadopoulos NG, Arakawa H, Carlsen KH, *et al.* International consensus on (ICON) pediatric asthma. *Allergy*. 2012;67:976-997.
 13. Holgate ST. Pathogenesis of asthma. *Clin Exp Allergy*. 2008 Jun;38(6):872-97. doi: 10.1111/j.1365-2222.2008.02971.x. PMID: 18498538.
 14. Knox AJ. How prevalent is aspirin induced asthma? *Thorax*. 2002;57:565-566. Wenzel S. Severe/fatal asthma. *Chest*. 2003;123:405S-410S.
 15. Robert F, William W. Asthma. *J Allergy and Clinical Immunology*. 2003;111(1):S49-S61. Busse WW, Lemanske RF Jr. Asthma. *N Engl J Med*. 2001;344:350-62.
 16. Relationship between asthma and rhinitis: Epidemiological, Pathophysiological And therapeutic aspects-C. Bergeronet al. *Allergy, Asthma and Clinical Immunology*. 2005;1:81-87.
 17. Wenzel S. Severe/fatal asthma. *Chest*. 2003;123:405S-410S.
 18. Sears MR. Epidemiology of asthma exacerbations. *Journal of Allergy and Clinical Immunology*. 2008 Oct 1;122(4):662-8.
 19. Vignola AM, J. Bousquet J, Tissue remodeling as a feature of Persistent asthma. *J Allergy Clin Immunology*. 2000;105:1041-53.
 20. Thomas AJ, Apiyasawat S, Spodick DH. Electrocardiographic detection of emphysema. *Am J Cardiol*. 2011;107:1090-2.
 21. Ulrik C, Peripheral eosinophil counts as a marker of disease activity in intrinsic and Extrinsic asthma. *Clin Exp Allergy*. 1995;25(9):820-7. *N Eng J Med*. 1975;292(22);1152-5.
 22. Horn B, Robin ED, Theodore J, Van Kessel A, Total eosinophil counts in management of Bronchial asthma.
 23. Platts Mills TA. The role of immunoglobulin E in allergy and asthma. *Am J Respir Crit Care Med*. 2006; 164:S1-S5.
 24. Borish L, Chipps B, Deniz Y, *et al.* Total serum IgE in a large cohort of patient with severe or difficult to treat asthma. *Ann allergy Asthma Immunology*. 2005;95:247-53
 25. Sanders C. The radiographic diagnosis of emphysema. *Radiol Clin North America*. 1991;29:1019.
 26. Snider GL Nosology for our day. Its application to COPD. *Am J Respir. Crit. Care Med*. 2003;167:678-683.
 27. Clinical approach to patients with COPD and Cardiovascular disease; Stephen I, Rennard *Am Thorac Soc*. 2005;2:94-100.
 28. COPD – Problems in diagnosis and measurement. *Eur. Respir. J*. 2003;21:Suppl. 41.
 29. Lieberman D, Lieberman D, Gelfer Y, *et al.* Pneumonic vs nonpneumonic acute exacerbations of COPD. *Chest* 2002;122:1264e70.
 30. Steer J, Norman EM, Afolabi OA, *et al.* Dyspnoea severity and pneumonia as predictors of in-hospital mortality and early readmission in acute exacerbations of COPD. *Thorax*. 2012;67:117e21.
 31. Costello R, Deegan P, Fitzpatrick M, McNicholas WT. Reversible hypercapnia in chronic obstructive pulmonary disease: a distinct pattern of respiratory failure with a favourable prognosis. *Am J Med*. 1997;102:239-244.