# AUDIT



# Initial management and investigations in acute exacerbation of chronic obstructive pulmonary disease: an audit

# C. J. Lawson

Emergency Department, Noble's Hospital, Isle of Man courtney.j.lawson@doctors.org.uk

# Abstract

**Introduction** Chronic obstructive pulmonary disease (COPD) affects three million people in England and Wales, including more than 5% of the over 65s. It is the country's fifth biggest killer, at 30,000 deaths per year. Severe exacerbations are the second commonest cause of emergency admissions, with 15% three-month mortality.

**Methods** The clinical practice of the Emergency Department (ED) on the Isle of Man was compared with UK best-practice guidelines regarding the initial management and investigations in acute exacerbation of COPD (AECOPD). The National Institute for Health and Care Excellence (NICE) *CG101* provides guidance for managing AECOPD. The evidence underpinning these guidelines was appraised and a retrospective audit of 40 patients in the ED was conducted.

**Results** Compliance to the use of air-driven nebulisers was uncertain due to insufficient documentation. Adequate arterial blood gas (ABG): 19 (47.5%). Chest radiograph (CXR): 39 (97.5%). Electrocardiogram (ECG): 37 (92.5%). Full blood count (FBC) plus urea and electrolytes (U&Es): 38 (95%). All pyrexial patients received blood cultures. Documentation of theophylline use was poor and patients on theophylline did not have levels measured.

**Conclusions** The initial management and investigations of AECOPD in the ED could be improved through research on nebuliser use, better documentation and implementation of departmental guidance for clinical decision-making.

Manchester Medical Journal, 2018 © The Authors.

This is an Open Access article published under the conditions of the Creative Commons Attribution-NonCommercial licence https://creativecommons.org/licenses/by-nc/4.0/ 1

MANCHESTER

Published by Manchester University Press, The University of Manchester Library and the Manchester Medical School http://dx.doi.org/10.7227/MMJ.0022 Manchester University Press

# Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive disorder of the airways characterised by airflow obstruction. The disease manifests as small-airway inflammation and damaged lung parenchyma with loss of elastic recoil. Most cases are attributed to cigarette smoking and the disease presents with varying severity. The prevalence in England and Wales is estimated at three million and the disease affects more than 5% of the over 65s.<sup>(1,2)</sup> The yearly mortality is 30,000; COPD is the country's fifth biggest killer.<sup>(3)</sup>

The most common symptoms of COPD are a productive cough, dyspnoea and chest tightness.<sup>(2)</sup> Exacerbations represent an acute worsening of symptoms. Severe exacerbations require hospitalisation and are the second most common cause of emergency admissions in England, with 15% of patients dying within three months of admission. The number of deaths attributed to respiratory disease is nearly double the EU average.<sup>(1,3)</sup>

The Isle of Man is a British Crown dependency located in the Irish Sea with a population of approximately 85,000. Demographically, 95.6% of the population is Caucasian, life expectancy is 81 years and almost 20% of the population is aged 65 and over.<sup>(4)</sup>

The jurisdiction of the National Institute for Health and Care Excellence (NICE) does not include the Isle of Man Emergency Department (ED). The ED does not have independent guidelines on managing acute exacerbation of COPD (AECOPD), therefore practice will be compared to the latest UK guidance, *NICE Clinical Guideline 101* (June 2010).<sup>(5)</sup> This was used to form the audit standards for the initial management and investigations in AECOPD:

- Nebulised pharmaceutical therapy must be prescribed driven by compressed air, not oxygen
- All patients must receive arterial blood gases (ABGs) with the fraction of inspired oxygen (FiO2) noted
- All patients must receive a plain chest radiograph (CXR)
- All patients must receive an electrocardiogram (ECG)
- All patients must receive full blood count (FBC) and renal function test (U&Es)
- Pyrexial patients must have blood cultures taken
- Patients on theophylline must have levels recorded at admission.

The target compliance was 100%, to reflect the guidance.

High-dose oxygen, including nebulised pharmaceutical therapy, can cause unpredictable hypercapnia in patients with AECOPD. Some patients are prone to repeated episodes of hypercapnic respiratory failure, whereas others are unaffected. Oxygen therapy controlled at a target of 88–92%

saturation pending ABGs is therefore recommended to reduce this risk. <sup>(6,7,8)</sup> Patients with a history of hypercapnic respiratory failure should carry an 'oxygen alert card' stipulating that nebulisers be air-driven. If compressed air is unavailable, oxygen-driven nebulisers should be limited to six minutes.<sup>(9)</sup> The implications of oxygen exposure through nebuliser use are underestimated in clinical practice.<sup>(10)</sup> Oxygen should be administered via nasal cannulae if required simultaneously with nebulisers.<sup>(5)</sup> The FiO2 using this method is relatively high, so patients with AECOPD may still be at risk of hypercapnic respiratory failure.<sup>(11)</sup> Air-driven nebulisers should always be preferred and nasal oxygen should only be supplied where clinically necessary.

Arterial blood gas tensions can have high prognostic predictive value in AECOPD. The partial pressure of carbon dioxide (PaCO2) calculated from arterial blood is an independent predictor of short-term mortality in AECOPD.<sup>(12)</sup> Acidosis is also a predictor of mortality in AECOPD.<sup>(13)</sup> Hypercapnia is an independent risk factor for predicting mortality.<sup>(14)</sup> There is good agreement for pH values between arterial and venous samples in patients with COPD; however, this does not apply for measurements of PaO2 or PaCO2.<sup>(15)</sup> FiO2 recording is mandatory for interpretative accuracy and a time lapse is required before ABGs are measured when FiO2 is changed. This is particularly important in diseases with ventilation/perfusion mismatch such as COPD.<sup>(16)</sup> Many guidelines recommend allowing 30 minutes for time to steady state in severe COPD, although only 10–16 minutes are required after a change in FiO2 to accurately record PaO2.<sup>(17)</sup> There is much clinical value in promptly recording and regularly monitoring ABGs in AECOPD.

CXR is useful for aiding diagnosis in AECOPD and identifying comorbidities. It is necessary to exclude other causes of dyspnoea, such as pulmonary oedema, pneumonia or pneumothorax. Additionally, COPD is responsible for 50–70% of secondary spontaneous pneumothorax cases, so identifying a possible pneumothorax is important.<sup>(7,18)</sup> Patients with COPD are twice as likely to have venous thromboembolic events as those without COPD. The prevalence of pulmonary embolism (PE) in patients suspected of AECOPD is 11.3%.<sup>(19)</sup> Patients with AECOPD are at increased risk of heart failure and a standardised approach for evaluating CXRs is superior at predicting two-year mortality than a routine approach.<sup>(20)</sup> CXR can reliably detect cardiomegaly on a postero-anterior (PA) film. However, AECOPD patients in the ED will receive a portable anteroposterior (AP) CXR. A reliable corrected cardiothoracic ratio (CTR) for AP CXRs can be calculated using a previous PA CXR.<sup>(21)</sup> CXRs at presentation of AECOPD have a range of important clinical applications and can highlight co-morbidities that may otherwise be undetected.

ECGs are commonly used in emergency departments and can identify cardiac co-morbidity in AECOPD. A predisposing factor for relapse

C. J. Lawson

in AECOPD is poor cardiovascular investigation and care. Identifying co-morbid patients and managing them appropriately may reduce this.<sup>(22)</sup> ECG detected 37% prevalence of heart disease (HD) in hospitalised AECOPD patients.<sup>(23,24)</sup> ECG is also an important tool for ruling out other causes of acute dyspnoea such as myocardial infarction and serious arrhythmias.<sup>(7)</sup> Therefore, its place in the initial investigations of AECOPD is well founded.

FBC can identify an infective aetiology of AECOPD, and U&Es are a marker of renal function to aid safe pharmaceutical prescribing.<sup>(7)</sup> However, leucocytosis may correlate poorly with bacterial pneumonia.<sup>(25)</sup> Erythrocyte count can detect anaemia as an alternative cause for dyspnoea or detect polycythaemia secondary to chronic hypoxia in COPD.<sup>(26)</sup> Serum urea recorded at presentation can predict inpatient mortality in AECOPD. Those with urea exceeding 7.35 mmol/L had 23.4% mortality risk, compared with an overall inpatient mortality of 15.5%.<sup>(27)</sup> FBC and U&Es are useful for baseline measurements and monitoring. They may support a diagnosis but should not be solely relied upon.

Blood cultures are indicated in pyrexial patients with AECOPD, although pyrexia only shows a trend towards the likelihood of blood culture testing positive, and 13% of bacteraemia cases are in afebrile patients.<sup>(28)</sup> Reports suggest pyrexia is not a significant predictor for positive blood culture, and positive blood cultures are not well utilised for guiding focused treatment.<sup>(29)</sup> Suspicion of bacteraemia should therefore encompass other clinical factors. This is reinforced by the lack of a universal definition of pyrexia.

Patients on theophylline therapy at presentation must have blood levels measured to avoid potential toxicity in case the drug is prescribed.<sup>(30)</sup>

# Aims

To investigate whether practice in the ED of a small island community in the British Isles is in line with UK best-practice guidelines for the initial management and investigations in AECOPD. This is measured through a retrospective audit of clinical records. Recommendations for improvement are made with consideration of potential barriers.

# Methods

An algorithm returned a list of patients who met the criteria 'adult ED attendances' AND 'arrival date and time', AND any of:

- diagnosis description OR free text contains 'COPD'
- diagnosis description OR free text contains 'COAD' (chronic obstructive airway disease)

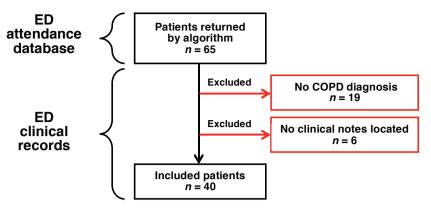


Figure 1: Flow chart of patient selection.

- diagnosis free text contains 'emphys'
- diagnosis free text contains 'bronchit'.

This supplied 65 patients from the four-month period September 2013– January 2014. The patients' physical ED clinical records were individually inspected and patients were included if the diagnosis was coded as 'exacerbation of COPD' or if a diagnosis of 'exacerbation of COPD' was written in the medical notes. A total of 19 patients were excluded due to absence of COPD diagnosis or coding error, 6 were excluded due to failure to locate clinical records. The final audit sample included 40 patients (Figure 1). The clinical records were analysed using a data collection tool.

# **Results**

The main results are summarised in Table 1.

#### Table 1: Main audit results

Audit standard	Compliance
Nebulised pharmaceutical therapy must be prescribed driven by compressed air, not oxygen	0%
All patients must receive ABGs with the FiO2 noted	47.5%
All patients must receive a chest X ray (CXR)	97.5%
All patients must receive an ECG	92.5%
All patients must receive an FBC and U&Es	95%
Pyrexial patients must have blood cultures taken	100%
Patients on theophylline must have levels recorded at admission	0%

# Discussion

# Standard 1: nebulised pharmaceutical therapy

The guidance that air-driven nebulisers should be used is clearly relevant to the ED as 34 (85%) patients received nebulisers (Figure 2). Compliance to this standard is subject to the availability of compressed air. The ED clinical notes for each patient have a designated prescription chart where the driving gas can be specified. None of the patients who received nebulised pharmaceutical therapy had the driving gas documented here. A total of 3 patients received oxygen-driven nebulisers and 1 patient received air-driven nebulisers, as documented in the written clinical notes (Figure 2). Therefore, in the remaining 30 cases the driving gas could not be determined.

Consequently, it is difficult to comment on the true compliance with the guideline. The audit did not collate data from any pre-hospital nebulised therapy that may have been administered. This may have influenced the decision to prescribe nebulisers in the ED, although the audit standard does not state that all patients must receive nebulisers. It can be inferred that there was 0% compliance with the standard that the driving gas should be specified in the prescription.

# Standards 2-5: ABG, CXR, ECG, FBC, U&Es

The ED has a near-point ABG analysis machine and the data entry menu permits input of the FiO2 value. A fifth of patients did not have ABG, and of those who did only 19 (60%) had the FiO2 noted (Figure 3), implying that 40% of ABGs were vulnerable to inaccurate interpretation. In those

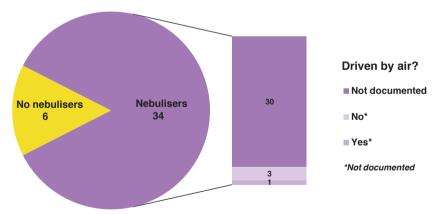
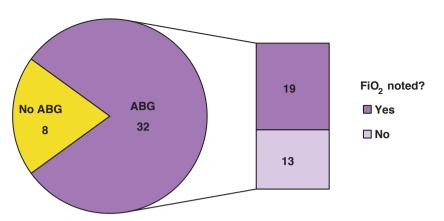


Figure 2: Patients who received nebulisers driven by air.

Patients who received nebulisers, n = 34 (85%). Driving gas of patients who received nebulisers, air: n = 1 (2.9%), oxygen: n = 3 (8.8%), not documented: n = 30 (88.2%). Driving gas was not documented in the prescription chart.



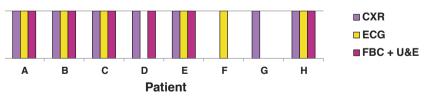


Patients who had ABG, n = 32 (80%). Patients who had ABG with FiO2 noted, n = 19 (47.5%).

who did not receive ABG there was no documented evidence of substitution by venous blood sampling.

Patients who received ABG had the analysis printout present with written confirmation in the clinical notes, whereas the remaining eight patients had neither. Some patients received more than one ABG, but the regularity of measurements was difficult to assess as the timestamp was often worn. The FiO2 was sometimes included in the data input but often written on the printout by hand; therefore, it is uncertain when this was recorded. A vital-signs chart including administered oxygen therapy was mostly present in the notes, but times did not always correlate with ABG measurements so this was not reliable for determining the FiO2. Additional investigations carried out in patients who did not have an ABG, including CXR, FBC and U&E, are shown in Figure 4. These are included in the discussion as it may be postulated that ABGs were omitted as they are more invasive.

Whilst five of the eight patients received all the other investigations, the





Patients who did not have ABG, n = 8 (20%). Patients who had all other investigations, n = 5 (62.5%). Patients who had ECG missing, n = 2 (25%). Patients who had CXR missing, n = 1 (12.5%). Patients who had FBC and U&Es missing, n = 2 (25%).

Manchester Medical Journal (2018) 1-13

remaining three had at least one missing. ECG was missing in two patients and CXR was missing in one patient. Both patients lacking ECG did have CXR, despite CXR requiring a request from the radiology department and involving exposure to ionising radiation. ECG is relatively safer and easier to carry out and would therefore be expected in these patients. Two patients were lacking FBC and U&Es even though CXR or ECG had been carried out, suggesting abnormalities were at least suspected and therefore supportive laboratory analysis and monitoring was indicated.

Figure 5 demonstrates the number of patients from the whole sample who received the four mandatory investigations in the ED. The findings do not account for the possibility that absent investigations were carried out following admission to a ward. The audit standards do not specify time constraints for investigations as this does not form part of the guidelines.

One patient did not have a CXR despite receiving nebulised pharmaceutical therapy, which suggests that there was clinical suspicion of a respiratory cause for presentation. ABG was also absent, indicating there may have been inadequate monitoring of markers of respiratory function. FBC and U&Es were not documented in the notes despite an unconfirmed aetiology of AECOPD and pharmaceutical management being initiated.

Several CXR reports remarked that the CTR could not be commented on due to the AP CXR, indicating that cardiomegaly was unlikely to be detected in these patients based on CXR findings alone.

ECG is readily available in the ED and can be operated by lower grade staff without specialist training, although interpretation must be performed by a doctor. Three patients did not have an ECG (see Figure 5),

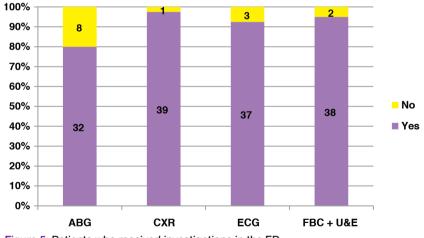


Figure 5: Patients who received investigations in the ED.

Patients who had ABG, n = 32 (80%). Patients who had CXR, n = 39 (97.5%). Patients who had ECG, n = 37 (92.5%). Patients who had FBC and U&E, n = 38 (95%).

C. J. Lawson

of which none were pyrexial and two did not receive nebulisers, suggesting that a cardiac presentation requiring ECG assessment should have been considered. Furthermore, all three patients had CXR, highlighting that there may have been a missed opportunity to identify cardiac co-morbidity that cannot be determined by AP CXR. The audit did not analyse the findings from the ECGs; therefore, the prevalence of co-morbidities that may predispose patients to relapse is beyond the scope of this study.

FBC and U&Es are frequently ordered in the ED and can be authorised by any doctor. Two patients did not receive these investigations, both of whom were afebrile and received either CXR or ECG, implying that a respiratory or cardiac presentation was considered more likely than a condition of infective aetiology. All patients who did receive FBC and U&Es had at least one other mandatory investigation, so these laboratory investigations were never solely relied upon.

#### Standard 6: blood cultures from pyrexial patients

Measurement of temperature is a simple clinical skill which forms an integral part of basic observations in the ED and pre-hospital care. Four (10%) patients in the audit were pyrexic, all of whom received blood cultures (figure 6), as well as CXR, ECG, and FBC and U&Es. Therefore, compliance with the audit standard was 100%, although the small sample size may question the significance of this finding.

The study did not account for patients who may have received antipyretics before observations were taken, which may in some cases lead to the omission of blood cultures in patients presenting with an infective aetiology. A significant weakness of this aspect of the audit was the lack

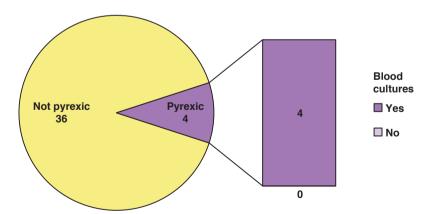


Figure 6: Patients who were pyrexic and had blood cultures.

Patients who were pyrexic, n = 4 (10%). Patients who were pyrexic and had blood cultures, n = 4 (100%).

9

of a quantitative definition of pyrexia in the audit standards. To overcome this, an arbitrary figure of 38.0°C was used. Unless the ED implements its own definition of pyrexia then individual cases are exposed to subjective interpretation. Furthermore, the study did not analyse whether afebrile patients received blood cultures.

## Standard 7: recording of theophylline levels on admission

Drug histories are handwritten in the ED clinical notes, included as a photocopy or omitted. Theophylline levels can be analysed from the serum-separating tube (SST) available in the ED. Only two patients (5%) were recorded as being on theophylline therapy. Both received nebulisers and ABG, implying the presence of respiratory distress, yet neither had theophylline levels measured.

However, there is only a small potential risk of theophylline toxicity if intravenous methylxanthines are prescribed. There was no evidence from the clinical documentation that patients were exposed to this risk. Drug history was often omitted, so the true number of patients on theophylline is unknown. Patients who were on theophylline had the drug history included as a photocopy of the repeat prescription, so there was no sign that this drug was specifically acknowledged.

# Conclusions

The ED could improve its clinical practice in the initial management and investigations of AECOPD. More research needs to be carried out into the use of nebulised pharmaceutical therapy in the ED. The carrying out of basic investigations is generally good, although there are some issues with adequate documentation. Protocols should be put in place to follow up underlying co-morbidities appropriately. Indications for blood culture could be clarified further to reduce bias from subjective interpretation. Awareness should be raised surrounding the potential risks of theophylline toxicity. Re-audit should be conducted and the audit standards should be adhered to for all patients presenting with AECOPD. Specific recommendations and potential barriers are described in Table 2.

# References

- Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. Lancet [Internet]. 2012 [cited 2014 Feb 11];379:1341–51. doi: 10.1016/S0140-6736(11)60968-9.
- 2 National Institute for Health and Care Excellence. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE guideline (CG101). London: NICE; 2008.

Table 2: Recommendations from the audit and potential barriers to change<sup>(1)</sup>

Recommendation	Potential barrier
Nebulisers should have the driving gas specified in the prescription chart of the ED notes	Lack of awareness
The $FiO_2$ should be entered into the ABG analysis data input form	Lack of awareness; assumption that it is not necessary
A protocol should be implemented for follow-up of co-morbidities in primary or secondary care, with a possible risk stratification for relapse	Ambiguity as to who is responsible; requires time and research; low detection rates of co-morbidities
Criteria for blood cultures should be implemented, with consideration of the definition of pyrexia	May conflict with hospital sepsis guidelines; requires time and research; may conflict with clinical judgement
All patients should have their theophylline status in the drug history of the ED notes	Lack of awareness; information may not be available

- 3 Department of Health. An outcomes strategy for chronic obstructive pulmonary disease (COPD) and asthma [Internet]. London: Department of Health; 2011 July [cited 2014 Feb 11]. Available from: www.gov. uk/government/uploads/system/uploads/attachment\_data/file/216139/ dh\_128428.pdf.
- 4 Central Intelligence Agency. The world factbook: Isle of Man [Internet]. Washington, DC: Central Intelligence Agency; 2016 [cited 2016 Feb 19]. Available from: www.cia.gov/library/publications/the-world-factbook/ geos/im.html.
- 5 National Institute for Health and Care Excellence. Chronic obstructive pulmonary disease: management of chronic obstructive pulmonary disease in adults in primary and secondary care (partial update), CG101. London: National Clinical Guideline Centre – Acute and Chronic Conditions; 2010.
- 6 O'Driscoll BR, Howard LS, Davison AG. Guideline for emergency oxygen use in adult patients. Thorax [Internet]. 2008 [cited 2014 Feb 11];
  63 (suppl VI):vi1–68. doi: 10.1136/thx.2008.102947.
- 7 Bauer T, Nilius G, Grüning W, Rasche K. Diagnose und Therapie der COPD-Exazerbation [Diagnosis and treatment of COPD exacerbation]. Medizinische Klinik-Intensivmedizin und Notfallmedizin. 2012;107(3):172–8. German.
- 8 Edwards L, Perrin K, Williams M, Weatherall M, Beasley R. Randomised controlled crossover trial of the effect on PtCO2 of oxygen-driven versus air-driven nebulisers in severe chronic obstructive pulmonary disease. Emerg Med J. 2012;29(11):894–8.
- 9 Bronchodilators; COPD. In: Joint Formulary Committee, British National Formulary, 67th ed [Internet]. London: British Medical

Association and Royal Pharmaceutical Society of Great Britain; [2014]. [cited 2014 Feb 11]. Available from: www.bnf.org/bnf/.

- 10 Pilcher J, Cameron L, Braithwaite I, Bowles D, Swain A, Bailey M, et al. Comparative audit of oxygen use in the prehospital setting, in acute COPD exacerbation, over 5 years. Emerg Med J. 2015;32(3):234–8.
- 11 Gea J, Orozco-Levi M, Gallart L. Fracciones inspiratorias elevadas de O2 con el uso del dispositivo convencional de nebulización de fármacos [Increased inspiratory oxygen fractions (FIO2) using a conventional drug delivery nebuliser]. Archivos de Bronconeumologia [Internet]. 2010 [cited 2014 Feb 11]; 46(5):230–7. Spanish. doi:10.1016/j.arbres.2010.02.002.
- 12 Samaria JK, Kumar H. Partial pressure of CO2 in arterial blood and serum random blood sugar at the time of admission are important mortality predictors in acute exacerbation of COPD. Lung India [Internet]. 2012 [cited 2014 Feb 11]; 29(suppl 1):S24–5. Available from: www.lungindia.com/backissues.asp.
- 13 Samaria JK, Hussain M, Kumar H. Factors affecting survival of patients admitted with acute exacerbation of chronic obstructive pulmonary disease. Lung India [Internet]. 2012 [cited 2014 Feb 11]; 29(suppl 1):S5. Available from: www.lungindia.com/backissues.asp.
- 14 Li J, Zhao H, Wang F, Dong H, Cai S. [Risk factors for in-hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease.] Zhonghua yi xue za zhi. 2013;93(18):1374–7. Chinese.
- 15 Lim B, Kelly A. A meta-analysis on the utility of peripheral venous blood gas analyses in exacerbations of chronic obstructive pulmonary disease in the emergency department. Eur J Emerg Med. 2010;17(5):246–8.
- 16 Thurnheer R. Stolpersteine bei der Beurteilung der arteriellen Blutgase [Fallacies in the assessment of arterial blood gases]. Therapeutische Umschau. 2013;70(8):473–9. German.
- 17 Weinreich U, Thomsen L, Hansen A, KjAergaard S, Wagner P, Rees S. Time to steady state after changes in FIO2 in patients with COPD. COPD. 2013;10(4):405–10.
- 18 Light RW. Secondary spontaneous pneumothorax in adults, ed. VC Broaddus [Internet]. Waltham, MA: UpToDate [updated 2015 Mar 31, cited 2016 Feb 19]. Available from: www.uptodate.com/contents/ secondary-spontaneous-pneumothorax-in-adults.
- 19 Dentali F, Arioli D, Pomero F, Re R, Di Micco P, Cattabiani C, et al. Acute pulmonary embolism or exacerbation of COPD? A challenging clinical dilemma: preliminary results of a large multicenter study. Eur J Intern Med. 2013 Oct;24(suppl. 1):e11–12.
- 20 Høiseth A, Omland T, Karlsson B, Brekke P, Søyseth V. Standardized evaluation of lung congestion during COPD exacerbation better identifies patients at risk of dying. Int J Chronic Obstr Pulm Dis. 2013 Dec 5;8:621–9.

C. J. Lawson

- 21 Chon S, Oh W, Cho J, Kim S, Lee S. Calculation of the cardiothoracic ratio from portable anteroposterior chest radiography. J Korean Med Sci. 2011; 26(11):1446–53.
- 22 Camp P, Burns J, Lane C, Sin D, Van Eeden S. Factors associated with rehospitalization within 14 days of hospital discharge for an acute exacerbation of chronic obstructive pulmonary disease. CHEST J. 2010;138(4):472.
- 23 Serrano S, Berenguer D, Oriol J, San Vicente L, Galofre N, Beltran G, et al. Prevalence of heart disease in patients hospitalized for an acute exacerbation of COPD: impact on clinical outcome. A 6 month follow-up study. Eur Respir J. 2011;38(suppl 55):547.
- 24 San Vicente L, Galofre N, Oriol J, Fernandez S, Kaplinsky E, Galvez E, et al. Impact of heart disease on the clinical outcome of patients hospitalized due to an acute exacerbation of COPD: a 12-month follow-up study. Eur J Heart Fail [Internet]. 2012 [cited 2014 Feb 11]; 11(suppl 1):S268. doi:10.1093/eurjhf/hss017.
- 25 Winter G, Marconcini ML, De Jesus CSC, Da Silva RM. Exacerbações infecciosas da doença pulmonar obstrutiva crônica [Infectious exacerbations of chronic obstructive pulmonary disease]. Revista Brasileira de Medicina [Internet]. 2012 Dec 3 [cited 2014 Feb 14]; 70(8–9). Portuguese. Available from: www.moreirajr.com.br/revistas. asp?fase=r003&id\_materia=5506.
- 26 Bourne S. Clinical review: COPD [Internet]. Twickenham: Haymarket Medical Media; 2012 Feb 8 [cited 2014 Feb 11]. Available from: http:// www.gponline.com/Clinical/article/1115137/Clinical-Review---COPD/.
- 27 Asiimwe A, Brims F, Andrews N, Prytherch D, Higgins B, Kilburn S, et al. Routine laboratory tests can predict in-hospital mortality in acute exacerbations of COPD. Lung. 2011;189(3):225–32.
- 28 Previsdomini M, Gini M, Cerutti B, Dolina M, Perren A. Predictors of positive blood cultures in critically ill patients: a retrospective evaluation. Croatian Med J. 2012;53(1):30–9.
- 29 Roque P, Oliver B, Anderson L, Mulrow M, Drachman D, Stapczynski S, et al. Inpatient utilization of blood cultures drawn in an urban ED. Am J Emerg Med. 2012;30(1):110–14.
- 30 Barr R, Rowe B, Camargo C. Methylxanthines for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2003 Apr 22;2:CD002168.