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Epidemiology, treatment, disposition and outcome of patients with acute exacerbation of COPD presenting to emergency departments in Australia and South East Asia: An AANZDEM study

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SUMMARY AT A GLANCE

Acute exacerbation of COPD is common in emergency departments (ED). This paper describes its epidemiology, clinical features, treatment and outcome. Patients commonly arrive by ambulance, have a high admission rate and significant in-hospital mortality. Compliance with evidence-based treatments and chronic management is sub-optimal affording opportunities to improve care.

ABSTRACT

Background and objective: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a common presentation to emergency departments (ED) but data regarding its epidemiology and outcomes are scarce. We describe the epidemiology, clinical features, treatment and outcome of patients treated for AECOPD in ED.

Methods: Planned sub-study of patients with an ED diagnosis of AECOPD identified in the Asia, Australia and New Zealand Dyspnoea in Emergency Departments (AANZDEM) study. AANZDEM was a prospective, interrupted time series cohort study conducted in 46 EDs in Australia, New Zealand, Singapore, Hong Kong and Malaysia over three 72-hour periods in May, August and October 2014. Primary outcomes were patient epidemiology, clinical features, treatment and outcomes (hospital length of stay (LOS) and mortality).

Results: 46 ED participated. There were 415 patients with an ED primary diagnosis of AECOPD (13.6% of the overall cohort; 95% CI 12.5-14.9%). Median age was 73 years, 60% male and 65% arrived by ambulance. Ninety-one percent had an existing COPD diagnosis. Eighty percent of patients received inhaled bronchodilators, 66% received systemic corticosteroids and 57% of those with pH<7.30 were treated with NIV. Seventy eight percent of patients were admitted to hospital, 7% to an intensive care unit. In hospital mortality was 4% and median LOS was 4 days (95% CI 2-7).

Conclusion: Patients treated in ED for AECOPD commonly arrive by ambulance, have a high admission rate and significant in-hospital mortality. Compliance with evidence-based treatments in ED is sub-optimal affording an opportunity to improve care and potentially outcomes.

Key words: COPD, exacerbation, emergency department, epidemiology, outcome, guideline

Short title: COPD in ED

INTRODUCTION

Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are common presentations to emergency departments (EDs).[1] Data from an United States administrative dataset analysis suggests that AECOPD account for approximately 0.8% of ED visits, that 49% of patients were hospitalized after an ED visit for COPD and that average length of stay was approximately 4 days.[1] European studies report admission rates of up to 65%.[2] There is minimal detailed data about demographic and clinical features, assessment, treatment and outcome of patients with AECOPD treated in EDs of Australasia and South East Asia.

Recent guidelines [3] recommend a number of treatments in the acute phase of care in order to optimize outcomes. These include the use of controlled oxygen therapy, inhaled bronchodilators, systemic corticosteroids, antibiotics if there is clinical, laboratory or chest xray (CXR) evidence of infection, the taking of a CXR, blood gas analysis for cases classified as more than mild and non-invasive ventilation (NIV) in patients with significant respiratory acidosis (pH<7.30). There is limited data regarding compliance with these elements in EDs. One recent single health service study from Australia reported compliance of 90% for administration of controlled oxygen therapy (if oxygen given), 87% for administration of inhaled bronchodilators, 79% for administration of systemic corticosteroids, 75% of administration of antibiotics if evidence of infection, 77% for taking of a blood gas in non-mild disease, 98% for taking of a CXR and 74% for administration of NIV if pH <7.30. [4] There is to date no data reporting compliance across multiple hospitals or a health system.

The aim of this project was to describe the demographic and clinical features, assessment, treatment and outcome of patients with AECOPD treated in EDs of Australasia and South East Asia and compliance with guideline recommended treatments.

METHODS

Study design and governance

This was a planned sub-study of a prospective, interrupted time series cohort study conducted in EDs in Australia, New Zealand, Singapore, Hong Kong and Malaysia the methodology of which has been previously published.[5,6] The project was overseen by a steering committee made up of researchers from Australia, New Zealand, Singapore and Hong Kong. The study sites have a combined annual ED census of 2,886,178 patients in 2014. Human research ethics approvals were obtained for all sites according to local requirements. In most jurisdictions patient consent for data collection was not required. Patient consent was required for some Queensland sites.

Site selection and participation

For the parent study, EDs were eligible to participate if they were an accredited ED according to local national criteria. Participation was by an expression of interest process. Directors of eligible EDs were contacted by email with an outline of the project and invited to participate. This planned sub-study included patients who had a final primary ED diagnosis of AECOPD.

Patient selection and data collection

Eligible patients for the parent study were consecutive adult patients presenting to ED with dyspnoea as a main symptom during the three 72-hour study periods (13-16 May 2014; 12-15 August 2014; 14-17 October 2014). This sub-study included those with a final primary ED diagnosis of AECOPD. These

dates were chosen to represent different seasons (autumn, winter and spring) in the region. Summer was not included due to funding limitations. The parent study used a specifically designed data collection instrument and data dictionary that was developed using an iterative process by the steering committee. The data form was piloted on a small sample of cases not included in the study period. Local data collectors were instructed that dyspnoea was considered a main symptom if it was listed as a symptom at presentation or triage (health systems varied slightly in how patient reception occurred).

Data was collected onto the validated data form by local clinician-investigators; nurses or doctors. Data was then entered as de-identified data into a password-secured central study database managed by the Clinical Informatics and Data Management Unit, Faculty of Medicine, Nursing and Health Sciences, Monash University.

Data collected included patient characteristics, co-morbidities, mode of arrival, usual medications, pre-hospital treatment as documented in ED clinical records, initial assessment (clinical assessment and vital signs), investigations performed in ED (laboratory tests, electrocardiogram (ECG), imaging, etc.) and results, treatment in the ED, ED diagnosis (diagnosis at conclusion of ED phase of care), disposition from ED, in-hospital outcome, length of stay for patients admitted to hospital (LOS) and final hospital diagnosis.

Outcomes of interest and analysis

The primary outcomes of interest for this study are the epidemiology and outcome (admission rate, mortality, LOS) of patients presenting to ED with dyspnoea who had a final primary ED diagnosis of AECOPD, overall and by region (South East Asia (SEA) and Australia/New Zealand (ANZ)).

Analysis is by descriptive statistics. A formal sample size calculation was not performed as this is largely a descriptive study.

RESULTS

Four hundred and fifteen patients met inclusion criteria with a median age of 73; 60% were male. Two hundred and eighty-one patients were from Australia, 121 from South-East Asia and 13 from New Zealand. Patients with an ED diagnosis of AECOPD made up 0.7% (95% CI 0.6-0.8%) of all ED attendances during the study period and13.6% (12.5%–14.9%) of the cohort of patients presenting with dyspnoea.[7]

Sixty-five percent of patients arrived at ED by ambulance. Demographic features and co-morbidity are summarized in Table 1. Of particular note, the vast majority of patients had a prior diagnosis of COPD (91%) and co-morbidity was common. Twenty four percent of patients were current or recent smokers (within the last year). Usual medications are also summarized in Table 1. Inhaled beta-sympathomimetic agents were commonly used and to a lesser extent inhaled corticosteroids. Oral steroids were only used by 16% and 14% of patients were on home oxygen therapy.

Median duration of symptoms prior to ED presentation was 3 days. Clinical features and investigations are summarized in Table 2. Of note, blood gas analysis (venous or arterial) was only performed in 55% of cases. The vast majority of patients underwent CXR (93%) and none had lung ultrasound imaging. Eighty percent of patients (95% CI 76-84%) received inhaled bronchodilators, 66% (95% CI 71-70%) received systemic corticosteroids and 57% (95% CI 41-73%) were treated with NIV if pH<7.30. (Table 3)

Seventy eight percent of patients were admitted to hospital (95% CI 74-82%), 7% (95% CI 5-10%) to an intensive care unit. In hospital mortality was 4% (95% CI 2-6%) and median LOS for patients admitted to hospital was 4 days (95% CI 2-7). (Table 3)

The principal final hospital diagnosis was COPD in 88% of cases (95% CI 85-91%). The main alternative primary diagnoses were lower respiratory tract infection (n=19, 4.6%), cardiac failure (n=7, 1.7%), asthma (n=5, 1.2%), malignancy (n=3, 0.7%) and acute coronary syndrome (n=2, 0.5%).

DISCUSSION

Patients with an ED primary diagnosis of AECOPD make up a significant proportion of ED caseload; a similar proportion to heart failure (15%) and asthma (12.7%).[7] They usually arrive by ambulance, have significant co-morbidities, more than three quarters require hospital admission and in-hospital mortality is 4%. Overall the regional cohorts were well matched for demographics and co-morbidity although it is notable that the smoking rate was significantly lower in SEA and cardiac failure was more common in ANZ.

We identified some deficits in investigation and treatment. Blood gas analysis to identify respiratory acidosis and hypercapnia is recommended by guidelines in all but mild cases.[8] Overall, just over half of patients had this test – two thirds of the ANZ cohort and a quarter of the SEA cohort. The lack of testing may result in under-diagnosis of respiratory acidosis that might benefit from treatment with biPAP and under-diagnosis of clinically significant hypercapnia which may have other implications for treatment, especially oxygen therapy. This study was not designed to identify reasons for not testing but these may include over-reliance on clinical assessment, lack of availability or cost of the test and failure to appreciate how the result of the test might influence management. Administration of uncontrolled oxygen therapy was sub-optimal, with approximately 14% of patients who were administered oxygen being given it by face mask. Interestingly, this was driven by ANZ sites suggesting significant difference in practice between regions. Administration of uncontrolled oxygen therapy runs the risk of depression of hypoxic respiratory drive in patients with chronic hypercapnia. Treatment with systemic corticosteroids and antibiotics was also different between the regions with ANZ having significantly higher rates of treatment with these agents. Reasons for this difference are unclear but potentially represent evidence-practice gaps.

Guidelines [8] also recommend that patients with AECOPD should receive both inhaled bronchodilators and systemic corticosteroids. That only 61% of patients received both is surprising. Systemic corticosteroids have been shown to reduce the likelihood of treatment failure and relapse at one month, shorten length of stay in hospital and give earlier improvement in lung function and symptoms.[8] Further work to improve implementation of evidence and guideline recommendation's is EDs is needed.

By definition, [8] patients attending an ED with AECOPD probably have at least moderate chronic disease. Recently published chronic treatment guidelines recommend bronchodilators as long term therapy for symptomatic disease with the addition of inhaled corticosteroids for patients with moderate disease and a history of exacerbations.[8] Given these recommendations, the reported use of bronchodilators and inhaled corticosteroids as chronic medications appears to be sub-optimal. This may represent a missed opportunity in primary care to optimize management with a view to preventing exacerbations and maximizing health outcomes.

The low use of NIV in patients with significant respiratory acidosis is of particular concern. The results reported may in fact over-estimate compliance with this therapy. The low rate of blood gas testing, especially in SEA, runs the risk of missed cases of respiratory acidosis which would reduce the proportion of eligible cases who received the therapy. Use of NIV has been shown to reduce in-hospital mortality (relative risk (RR) 0.66, 95% CI 0.48 to 0.89) and requirement for endotracheal intubation (RR 0.52, 95% CI 0.36 to 0.75).[9] Reasons for the low use are unclear. Some may be patient refusal of this treatment, as it can be difficult for some patients to tolerate. In our experience, this is quite uncommon. Other potential reasons are lack of awareness of the effectiveness of this treatment, lack of structured assessment to

identify eligible patients, lack of appropriate equipment and lack of confidence by staff (nursing and medical) in its use.

Overcoming evidence-practice gaps is not easy. They could potentially be overcome by structured assessment and treatment pathways and specific training in the use of NIV. Using a treatment proforma approach, previous studies have demonstrated improvements in categorization of respiratory failure, administration of controlled oxygen therapy and appropriate referral for NIV and improved compliance with defined therapies.[10,11] An alternative approach to improving compliance could be the use of a clinical informatics approach such as computer-assisted decision support, although this approach requires significant infrastructure to support it.

There have been three other reports regarding compliance with the complete COPD-X guideline [3] (or similar) bundle of care in EDs. All identified use of NIV in eligible patients as a major evidence-practice gap.[4,12,13] Two identified administration of antibiotics in patients with evidence of infection as requiring improved compliance and administration of systemic corticosteroid [4,12] while one reported a gap in appropriate use of blood gas analysis.[4] Another North American study [14] also reported low rates of blood gas analysis (48%) and antibiotic administration (28%).

That the ED primary diagnosis of AECOPD was confirmed in 88% of cases represents high accuracy of ED diagnosis. Given the high co-morbidity burden of the cohort (particularly co-existent cardiac failure), the interplay between these co-morbidities (especially between lower respiratory tract infection and

AECOPD) and the fact that ED diagnoses are often being made on incomplete data, this discrepancy probably simply reflects the reality of ED clinical practice for this complex patient group.

There are some limitations that should be considered when interpreting these results. We did not confirm diagnosis or severity using spirometry. This was usually not available in the participating EDs and is rarely used in acute ED practice. Rather we relied on the ED clinician's diagnosis of AECOPD, reflecting real world practice. Data may have been collected retrospectively so may be subject to the risk of data omission.[15] Local data collectors were not blinded to the aims of the project which may have introduced bias. We did not collect reasons why specific treatments or assessments were not used. There may have been legitimate reasons for their omission so our data may be an under-estimate of compliance with recommended treatments.

In conclusion, patients treated in ED for AECOPD commonly arrive by ambulance, have a high admission rate and significant in-hospital mortality. Compliance with evidence-based treatments in ED and in chronic management is sub-optimal affording opportunities to improve care and potentially outcomes.

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A list of COLLABORATORS (AANZDEM Study group members**)** is available in Supplementary Appendix S1.

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TABLES

Table 1. Patient characteristics (ANZ= Australian & New Zealand, SEA= Hong Kong, Singapore & Malaysia)

Variable	Overall results (N=415)	ANZ	ANZ missing data	SEA	SEA missing data	P value
Age (median, IQR)	73 (65-81)	73 (64-81)	0	74, 66-82	0	0.25
Gender (male, N, %, 95% CI)	249 (60%, 55-65%)	150, 51%	0	99, 82%	0	<0.0001
Region						
Australia and New Zealand	294 (71%, 66-75%)		-		-	
Asia	121 (29%, 25-34%)		-		-	
Co-morbidities (N, %, 95% CI)						
Previous diagnosis COPD	375 (91%, 87-93%)	261, 89%	1	114, 94%	0	0.10
Hypertension	215 (52%, 47-57%)	160, 55%	3	55, 46%	0	0.08
Dyslipidaemia	123 (30%, 25-34%)	99, 34%	2	24, 20%	0	0.004
Ischaemic heart disease	102 (25%, 21-29%)	76, 26%	3	26, 22%	0	0.32
Active or recent smoker	98 (24%, 20-28%)	79, 27%	3	19, 16%	0	0.01
Diabetes	78 (19%, 15-23%)	59, 20%	3	19, 16%	1	0.30
Cardiac failure	73 (18%, 14-22%)	61, 21%	3	12, 10%	0	0.008
Chronic renal disease	47 (11%, 9-15%)	36, 12%	3	11, 9%	0	0.34
Active malignancy	22 (5%, 3-8%)	14, 5%	4	8, 7%	0	0.46
Pulmonary embolism	17 (4%, 3-7%)	17, 6%	3	0, 0%	0	0.005
Chronic medications (N, %, 95% CI)						
Inhaled beta-sympathomimetics	308 (74%, 70-78%)	219, 75%	1	89, 74%	0	0.80
Inhaled anticholinergics	231 (56%, 51-60%)	163, 55%	0	68, 56%	0	0.89
Inhaled corticosteroids	211 (51%, 46-56%)	152, 52%	1	59, 49%	0	0.56
Diuretic	89 (22%, 18-26%)	75, 26%	2	14, 12%	0	0.002
Oral corticosteroids	68 (16%, 13-20%)	53, 18%	2	15, 12%	0	0.15
Home oxygen	57 (14%, 11-18%)	42, 14%	2	15, 12%	1	0.59
Xanthines	34 (8%, 6-11%)	7, 2%	2	27, 22%	0	<0.0001
Leukotriene receptor antagonists	6 (1%, 0.6-3%)	3, 1%	2	3, 3%	0	0.48
Mode of arrival (ambulance, N, %, 95% CI)	260 (65%, 60-69%)	187, 64%	9	76, 60%	3	0.73

Table 2. Clinical features

Variable	Result (N=415)	Missing data
Duration of symptoms (median, IQR)	3 (1-7)	17
Ability to speak		132
None	6 (2%, 0.9-5%)	
Phrases	62 (22%, 17-27%)	
Sentences	121 (43%, 37-49%)	
Normal	94 (33%, 28-39%)	
Pulse rate (median, IQR)	99, 84-112	12
Pulse rate e 120 (N, %, 95% CI)	68 (17%, 13-21%)	
Respiratory rate (median, IQR)	25, 22-30	18
Respiratory rate e30 (N, %, 95% CI)	101 (25%, 21-30)	
Blood pressure (median, IQR)	139, 120-157	13
<100mmHg (N, %, 95% CI)	9 (2%, 1-4%)	
Temperature <35 or e38.5 C (N, %, 95% CI)	17 (4%, 3-7%)	23
Oxygen saturation on air		127 (117 were on oxygen at initial assessment)
<94% (N, %, 95% CI)	158 (55%, 49-61%)	
<90% (N, %, 95% CI)	87 (30%, 25-36%)	
Auscultation (N, %, 95% CI)		28
Wheeze	193 (50%, 45-55%)	
Widespread rhonchi	64 (17%, 13-21%)	
Basal crepitations	45 (12%, 9-15%)	
Normal	41 (11%, 8-14%)	
Widespread crepitations	23 (6%, 4-9%)	
Local rhonchi/ bronchial breathing	16 (4%, 2-7%)	
Signs suggestive of pleural effusion	4 (1%, 0.3-3%)	
Signs suggestive of pneumothorax	1 (0.2%, 0.01-2%)	

Table 3: Investigation, treatment and outcome (ANZ= Australian & New Zealand, SEA= Hong Kong, Singapore & Malaysia)

Variable	Overall result (N=415)	ANZ	ANZ missing data	SEA	SEA missing data	P value
Investigations						
White cell count >15 (N, %, 95% CI)	48 (14%, 11-18%)	38, 14%	21	10, 15%	56	0.30
Blood gas taken (venous or arterial) (N, %, 95% CI)	229 (55%, 50-60%)	200, 68%	-	29, 24%	-	<0.0001
pCO2>50mmHg (N, %, 95% CI)	65 (28%, 23-35%)	52, 26%	-	14, 48%		0.03
pH <7.30 (N, %, 95% CI)	38 (17%, 12-22%)	29, 15%	-	9, 31%		0.03
Imaging (N, %, 95% CI)						
Chest xray	388 (93%, 91-96%)	278, 95%	0	110, 91%	0	0.17
Ventilation perfusion scan or CTPA	8 (2%, 1-4%)	7, 2%	0	1, 0.8%	0	0.27
Lung ultrasound	0 (0%, 0-1%)	0, 0%	0	0, 0%	0	1
Oxygen therapy						
Initial oxygen therapy (N, %, 95% CI)			0		0	<0.0001 (omnibus Chi Square)
None	158 (38%, 33-43%)	120, 41%		38, 31%		
Low flow nasal prongs	115 (28%, 24-32%)	87, 30%		28, 23%		
Face mask	58 (14%, 11-18%)	54, 18%		4, 3%		
Venturi-type system	28 (7%, 5-10%)	8, 3%		20,17%		
Non-rebreather	12 (3%, 2-5%)	3, 1%		9, 7%		
Non-invasive ventilation (CPAP or BiPAP)	12 (3%, 2-5%)	12, 4%		0		
Mechanical ventilation	1 (0.2%, 0.01-2%)	0		1, 0.8%		
High flow nasal prongs	0 (0%, 0-1%)	0		0		
Oxygen given but mode unknown	30 (7%, 5-10%)	9, 3%		21,17%		
Oxygenation mode used at any time in ED (N, %, 95% CI)			0		0	
Non-invasive ventilation (CPAP or BiPAP)	46 (11%, 8-15%)	39, 13%		7, 6%		0.02
High flow nasal prongs	7 (2%, 0.7-4%)	7, 2%		0		0.09
Mechanical ventilation	4 (1%, 0.3-3%)	1, 0.3%		3, 2%		0.08

Therapy						
Inhaled beta sympathomimetic (N, %, 95% CI)	332 (80%, 76-84%)	226, 77%	2	106, 88%	0	0.01
Inhaled anticholinergic agent (N, %, 95% CI)	226 (55%, 50-60%)	159, 55%	2	67, 55%	0	0.86
Inhaled bronchodilator (beta-sympathomimetic or anticholinergic) (N, %, 95% CI)	332 (80%, 76-84%)	226, 77%	2	106, 88%	0	0.01
Oral corticosteroid (N, %, 95% CI)	178 (43%, 38-48%)	151, 52%	2	27, 22%	0	<0.0001
Intravenous corticosteroid (N, %, 95% CI)	110 (27%, 23-31%)	68, 23%	3	42, 35%	0	0.02
Systemic corticosteroid (Oral or IV) (N, %, 95% CI)	271 (66%, 61-70%)	205, 70%	2	67, 55%	0	0.006
Both inhaled bronchodilators and systemic corticosteroids (N, %, 95% CI)	253 (61%, 56-66%)	188, 64%	2	65, 54%	0	0.04
Inhaled bronchodilators without systemic steroids (N, %, 95% CI)	79 (19%, 16-23%)	38, 13%	3	41, 34%	0	<0.001
Systemic corticosteroids without bronchodilators (N, %, 95% CI)	18, 5%	16, 4%	3	2, 2%	0	0.08
Neither inhaled bronchodilators or systemic corticosteroids (N, %, 95% CI)	62 (15%, 12-19%)	49, 17%	3	13, 11%	0	0.13
Antibiotic (N, %, 95% CI)	200 (49%, 44-53%)	170, 58%	3	30, 25%	0	<0.0001
NIV if pH>7.30 (N=38) (N, %, 95% CI)	22 (57%, 41-73%)	18, 62%	0	4, 44%	0	0.28
Outcome						
Disposition (N, %, 95% CI)						0.54 (omnibus Chi Square)
Inpatient ward (excluding ICU)	297 (72%, 67-76%)	202, 69%	0	93, 77%	0	

Home (including via an ED observation unit)	80 (19%, 16-23%)	62, 21%	0	20, 17%	0	
ICU	28 (7%, 5-10%)	23, 8%	0	5, 4%	0	
Transfer	9 (2%, 1-4%)	6, 2%	0	3, 3%	0	
Death in ED	1 (0.2%, 0.1-2%)	1, 0.3%	0	0	0	
In-hospital mortality (N, %, 95% CI)	16 (4%, 2-6%)	9, 3%	0	7, 6%	0	0.19
Length of stay for patients admitted to hospital (days, median, IQR)	4, 2-7	5	0	4	0	0.04

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