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ORIGINAL RESEARCH

Epidemiology, treatment and outcome of patients with lower respiratory tract infection presenting to emergency departments with dyspnoea (AANZDEM and EuroDEM studies)

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Abstract

Objective: Lower respiratory tract infection (LRTI) is a frequent cause of

dyspnoea in EDs, and is associated with considerable morbidity and mortality. We described and compared the management of this disease

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Key findings

- We described and compared European and Oceania/SEA populations of patients presenting to EDs with dyspnoea and a diagnosis of LRTI.
- In Europe, more patients with LRTI presented with cardiorespiratory comorbidities. They received more adjunct therapies and had a higher ICU admission rate than patients from Oceania/SEA.

in Europe and Oceania/South-East Asia (SEA) cohorts.

Methods: We conducted a prospective cohort study with three time points in Europe and Oceania/SEA.

We included in this manuscript patients presenting to EDs with dvspnoea and a diagnosis of LRTI in ED. We collected comorbidities, chronic medication, clinical signs at arrival, laboratory parameters, ED management and patient outcomes. Results: A total of 1389 patients were included, 773 in Europe and 616 in SEA. The European cohort had more comorbidities including heart failure, obesity, chronic chronic obstructive pulmonary disease and smoking. Levels of inflammatory markers were higher in Europe. There were more patients with inflammatory markers in Europe and more hypercapnia in Oceania/SEA. The use of antibiotics was higher in SEA (72.2% vs 61.8%, P < 0.001) whereas intravenous diuretics, non-invasive and invasive ventilation were higher in Europe. Intensive care unit admission rate was 9.9% in Europe cohort and 3.4% in Oceania/SEA cohort. ED mortality was 1% and overall inhospital mortality was 8.7% with no differences between regions.

Conclusions: More patients with LRTI in Europe presented with cardio-respiratory comorbidities, they received more adjunct therapies and had a higher intensive care unit admission rate than patients from Oceania/ SEA, although mortality was similar between the two cohorts.

Key words: *dyspnoea, emergency, epidemiology, lung disease.*

Introduction

Shortness of breath is a common reason for presentation to EDs. A lower respiratory tract infection (LRTI) is responsible for approximately 20% of patients presenting to the ED with dyspnoea.¹ It is strongly associated with mortality, as up to 40% of patients who die during their hospital stay are diagnosed with LRTI.^{1,2}

LRTI is defined as an acute illness with cough as the main symptom, at least one additional lower respiratory tract symptom and no alternative explanation.³ The management of LRTI depends on severity of the infection, demographics and comorbidities (such as diabetes, cardiovascular disease and obstructive pulmonary disease). The diagnosis may require a new infiltrate on chest radiography and respiratory symptoms, sometimes atypical (especially in elderly patients). Microbiological investigations can confirm the diagnosis.⁴ The pathogen identified is viral (e.g. influenza) in approximately half or bacterial in about 20% of patients.⁵ The management of communityacquired pneumonia (CAP) is based on antibiotics and ventilatory support, using mechanical ventilation in extreme situations. An estimation of 915 900 episodes of CAP occurs in adults ≥65 years each year in the USA.⁶

The aim of this planned substudy was to describe and compare the demographic and clinical features, treatment and outcome of patients attending EDs across Europe and Oceania/South-East Asia (SEA) with a primary complaint of dyspnoea and a LRTI diagnosis.

Methods

We conducted an international multicentre prospective, observational study at three time points. The present study was designed to evaluate diagnosis, treatment and outcome of patients presenting to the ED with dyspnoea. The protocol (NCT02060799) was described in previous publications^{1,7,8} and included 66 EDs in Europe and 46 in Oceania/SEA during three 72-h study periods (winter, autumn and spring 2014 in each region).

This planned substudy presents an analysis of patients who were diagnosed with LRTI in the ED. LRTI in our work includes acute exacerbations of bronchiectasis and CAP. The diagnosis of LRTI was established by the emergency physician caring for the patient. We retained the main diagnosis of LRTI in ED for our analysis. Data collected were patient characteristics, comorbidities, chronic medication, clinical signs at arrival, laboratory parameters, ED management and patient outcomes.

Outcomes of interest for this work were differences in epidemiology, management and outcomes between European (EuroDEM) and Oceania/ SEA (Asia, Australia and New Zealand Dyspnoea in Emergency Departments [AANZDEM]) study cohorts.

Statistical analysis

Results are presented as frequencies or as median with interquartile ranges. Categorical variables were analysed using the χ^2 test or Fisher's exact test as appropriate. Numerical variables were analysed using the *t* test and the Wilcoxon test (non-parametric variables). A *P*-value of less than 0.05 was considered as statistically significant. All data analyses were conducted using SAS version 9.1 software (SAS Institute, Cary, NC, USA).

The study was performed in accordance with the Declaration of Helsinki. Ethics committee approvals were obtained for all sites according to local requirements, and patient consent for data collection was obtained if requested.

Results

A total of 1389 patients with LRTI were included, 616 from SEA and 773 from Europe, representing, respectively, 20.2% and 30.6% of AANZDEM and EuroDEM cohorts.⁸ The median age was 71 (57-82) years and 52.1% were males. The median duration of shortness of breath was 3 (1-6) days. Patient characteristics are presented in Table 1. Some comorbidities were significantly higher in the European population, such as chronic heart failure (23.6% vs 12.4%), obesity (16.8% vs 6.4%), chronic obstructive pulmonary disease (COPD) (34.9% vs 21.4%), dysfunction cognitive (12.3% vs 8.5%) and smoking (24.4% vs 10.8%). The mean of comorbidities per patient was 2.7 (SD ± 2.0) without significant difference between the cohorts (2.5 [SD ± 2.0] in SEA and 2.8 [SD ± 2.0] in EuroDEM).

Vital signs and clinical signs at admission are reported in Table 2. Only 22.3% had temperature disturbance (fever or hypothermia). Rales were the most representative sign of LRTI (55.1%) and 17.8% had normal pulmonary auscultation. Rales, wheezing and rhonchi were significantly

	Total	AANZDEM	EuroDEM	P-value
<i>n</i> (%)	1389	616 (44.3)	773 (55.7)	
Age (years), median (Q1-Q3)	71 (57–82), missing data $n = 6$	72 (56-83)	71 (57-81)	0.624
Male, <i>n</i> (%)	721 (52.1), missing data $n = 6$	326 (52.9)	395 (51.5)	0.599
Duration of symptoms (days), median (Q1–Q3)	3 (1–6), missing data <i>n</i> = 134	3 (1–7)	3 (1–7)	0.986
Comorbidities, <i>n</i> (%)				
Chronic heart failure	246 (18.4), missing data <i>n</i> = 55	76 (12.4)	170 (23.6)	< 0.001
Diabetes mellitus	312 (23.1), missing data <i>n</i> = 36	147 (23.9)	165 (22.3)	0.483
Hypertension	635 (47.0), missing data $n = 37$	275 (44.8)	360 (48.8)	0.143
Coronary artery disease	310 (23.3), missing data $n = 61$	146 (23.8)	164 (22.9)	0.705
AF/flutter	220 (16.3), missing data <i>n</i> = 42	92 (15)	128 (17.4)	0.229
Obesity	157 (12.0), missing data $n = 78$	39 (6.4)	118 (16.8)	< 0.001
Chronic obstructive pulmonary disease	386 (28.8), missing data $n = 47$	131 (21.4)	255 (34.9)	< 0.001
Chronic renal disease	168 (12.4), missing data $n = 37$	74 (12.1)	94 (12.7)	0.719
Cognitive dysfunction	144 (10.6), missing data $n = 31$	52 (8.5)	92 (12.3)	0.022
Active malignancy	116 (8.6), missing data <i>n</i> = 44	53 (8.7)	63 (8.6)	0.966
Smoker	235 (18.0), missing data $n = 82$	66 (10.8)	169 (24.4)	< 0.001
Asthma	228 (16.8), missing data $n = 34$	105 (17.2)	123 (16.6)	0.768
Prior PE	39 (2.9), missing data <i>n</i> = 39	15 (2.5)	24 (3.3)	0.382
Chronic medication use, n (%)				
Beta-blockers	349 (25.2), missing data $n = 3$	122 (19.9)	227 (29.4)	< 0.001
ACE inhibitors or ARBs	408 (29.5), missing data $n = 4$	169 (27.6)	239 (30.9)	0.180
Aldosterone antagonists	58 (4.2), missing data $n = 5$	30 (4.9)	28 (3.6)	0.235
Cardiac glycosides	43 (3.1), missing data <i>n</i> = 5	23 (3.8)	20 (2.6)	0.210
Diuretics	369 (26.6), missing data $n = 3$	132 (21.5)	237 (30.7)	0.001
Inhaled beta-2 agonists	411 (29.7), missing data <i>n</i> = 4	172 (28.1)	239 (30.9)	0.255
Oral steroids	130 (9.4), missing data <i>n</i> = 4	50 (8.2)	80 (10.3)	0.167
Home oxygen	63 (4.5), missing data $n = 4$	16 (2.6)	47 (6.1)	0.002
Mode of arrival, n (%)				
By ambulance†	754 (55.1), missing data $n = 21$	330 (54.8)	424 (55.4)	0.843

TABLE 1. Patient characteristics

†Data are presented as number (%) or median (interquartile range). ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; PE, pulmonary embolism.

more frequent in the EuroDEM cohort.

Laboratory parameters at admission were reported in Table 3. Median white blood cell count (WBCC) was 10.6 (8.0–14.6) g/L and leucocytosis (WBCC >12 g/L) was found in 37.4% of patients. Median C-reactive protein was 20 (5–85) mg/dL and was significantly higher in the EuroDEM cohort (41 [12–114] mg/dL vs 7 [2–23] mg/dL, P < 0.001). Blood gas abnormalities included acidosis (pH <7.3) in 9.2% of patients and hypercapnia (PaCO₂ ≥50 mmHg) in 18%. Hypercapnia was found in 23.8% of patients in the AANZDEM cohort and in 15.5% of patients in the EuroDEM cohort (P < 0.001).

The ED management included antibiotics (66.5%), inhaled beta-2

agonists (40.1%), corticosteroids intravenous or oral (23.3%), intravenous diuretics (13.1%). The use of mechanical ventilation was 1.4%. Two-thirds (66.7%) of patients were admitted to a ward, 28.3% of patients were discharged home, 6.8% were admitted to intensive care and 1% died in ED. The in-hospital mortality was 8.7% without statistical difference between the two

	Total	AANZDEM	EuroDEM	P-value
Vital signs at admission				
SBP (mmHg), median (Q1–Q3)	132 (117–150), missing data $n = 29$	133 (116–152)	132 (118-150)	0.329
SBP <100 mmHg, <i>n</i> (%)	92 (6.8)	42 (7.0)	50 (6.6)	0.770
Heart rate (/min), median (Q1– Q3)	96 (82–110), missing data <i>n</i> = 21	97 (81–110)	96 (82–110)	0.321
Heart rate >120/min, <i>n</i> (%)	177 (12.9)	81 (13.3)	96 (12.6)	0.689
Respiratory rate (cycles/min), median (Q1–Q3)	22 (18–28), missing data <i>n</i> = 125	22 (20–28)	22 (18-28)	0.024
Respiratory rate >30 cycles/min, n (%)	190 (15.0)	94 (15.6)	96 (14.5)	0.597
SpO ₂ <90%, <i>n</i> (%)	247 (20.0), missing data <i>n</i> = 154	90 (18.2)	157 (21.2)	0.201
Temperature <35 or >38°C, n (%)	292 (22.3), missing data <i>n</i> = 77	152 (25.3)	140 (19.7)	0.014
Clinical signs at admission, n (%)				
Confusion	108 (8.0), missing data $n = 33$	30 (4.9)	78 (10.4)	< 0.001
Peripheral oedema	228 (20.6), missing data <i>n</i> = 284	82 (22.2)	146 (19.9)	0.373
Rales	721 (55.1), missing data <i>n</i> = 80	282 (47.6)	439 (61.3)	< 0.001
Wheezing	317 (24.9), missing data <i>n</i> = 118	104 (17.5)	213 (31.4)	< 0.001
Rhonchi	314 (24.9), missing data <i>n</i> = 129	80 (13.5)	234 (35.1)	< 0.001
Pulmonary auscultation normal†	239 (17.8), missing data <i>n</i> = 47	125 (20.3)	114 (15.7)	0.029

TABLE 2. Clinical signs at presentation to the ED

†Data are presented as number (%) or median (interquartile range). SBP, systolic blood pressure; SpO₂, arterial blood oxygen saturation.

cohorts. Some differences were noticed in the ED management between the two cohorts (Table 4). At discharge, the diagnosis of LRTI was retained in 75.6% of hospitalised patients, respectively, 83.7% (AANZDEM) and 68.8%(EuroDEM) (P < 0.001).

Discussion

This subgroup analysis described and then compared the clinical presentation, investigations and management of patients attending the ED with dyspnoea and a diagnosis of LRTI. It was noted almost a quarter (22%) had an abnormal temperature and 18% had normal auscultation. probably This result may be explained by the difference in temperature measurement methods and by the age of our population. Indeed, increased body temperature could be absent in elderly patients.9 More European patients had comorbidities, including smoking, COPD, obesity, chronic heart failure and cognitive dysfunction. Rales, wheezing and rhonchi were found in the majority of European patients, possibly because of the high proportion of smokers and COPD.

There were some differences in ED management between the two cohorts. Non-invasive ventilation and mechanical ventilation were used more often in Europe, as were intravenous diuretics and inhaled beta-2 agonists. The use of antibiotics was significantly higher in the Oceania/SEA cohort. This difference in antibiotics management is difficult to interpret because of the lack of microbiological results. It is possible that the difference is partially explained by a poor concordance with national CAP guidelines in Australasia.¹⁰ Approximately 10% of European patients required intensive

care unit (ICU) admission as described in other studies.^{11,12} Only 3.4% of Oceania/SEA patients were admitted to ICU. However, since the mortality rate in ED and in-hospital was similar between the two cohorts, this difference in ICU admission may reflect a different threshold for admission or indicate a different availability of intensive care beds between Europe and Oceania/SEA. Indeed, there are some differences in the guidelines of management of LRTI in Europe³ and Australia.¹³ In the decision Europe, of hospitalisation remains a clinical decision and is validated against the CRB 65 score. This score is the most practical without biological results. The ICU admission depends on the local setting and facilities. Any score is recommended and the decision is based on clinical state as acute respiratory failure, septic shock and radiographic extension of infiltrates. In

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Laboratory parameters at admission	Total	AANZDEM	EuroDEM	P-value
Creatinine (µmol/L), median (Q1–Q3)	82 (65–109), performed <i>n</i> = 912 (65.7%)	84 (66–109)	79 (64–105)	0.007
Sodium (mmol/L), median (Q1–Q3)	138 (135–140), performed <i>n</i> = 1226 (88.3%)	137 (135–140)	138 (135–140)	0.274
Sodium ≤130, <i>n</i> (%)	92 (7.5)	43 (8.3)	49 (7.0)	0.429
Potassium (mmol/L), $4.1 (3.8-4.5)$, performed $n = 1189 (85.6\%)$ median (Q1–Q3)		4.1 (3.8–4.5)	4.2 (3.8–4.5)	0.092
Blood glucose (mmol/L), median (Q1–Q3)	7.0 (5.8–8.9), performed <i>n</i> = 594 (42.8%)	6.9 (5.8–9.0)	7.0 (5.8–8.7)	0.143
C-reactive protein (mg/dL), median (Q1–Q3)	20 (5–85), performed <i>n</i> = 796 (57.3)	7 (2–23)	41 (12–114)	<0.001
C-reactive protein >10 mg/dL, <i>n</i> (%)	498 (62.6)	121 (40.1)	377 (76.3)	< 0.001
pH, median (Q1–Q3)	7.41 (7.36–7.46), performed $n = 736$ (53.0)	7.4 (7.35–7.44)	7.42 (7.36–7.46)	< 0.001
pH <7.3, n (%)	68 (9.2)	29 (11.6)	39 (8.0)	0.107
PaCO ₂ (mmHg), median (Q1–Q3)	38 (32–46), performed <i>n</i> = 433 (31.2)	41 (35–49)	37 (31–45)	0.001
$PaCO_2 \ge 50 \text{ mmHg},$ n (%)	78 (18.0)	31 (23.8)	47 (15.5)	0.039
WBC count (g/L), median (Q1–Q3)	10.6 (8.0–14.6), performed <i>n</i> = 990 (71.3)	10.4 (7.7–14.1)	11.0 (8.0–15.2)	0.287
WBC count >12 g/L, <i>n</i> (%)	370 (37.4)	182 (35.2%)	188 (39.7%)	0.140
Haemoglobin (g/dL), median (Q1–Q3)	13.0 (11.5–14.4), performed <i>n</i> = 1171 (84.3)	13.1 (11.5–14.4)	13.0 (11.4–14.3)	<0.001
Haemoglobin <10 g/dL, <i>n</i> (%)†	115 (9.8)	56 (10.6)	59 (9.2)	0.413

umber (76) or median (interquartile range).

Australasia, SMART-COP and CORB scores are recommended as tools of risk assessment. Patients with a CORB score of 0 are assigned into mild CAP (ambulatory treatment), 1 into moderate CAP and ≥2 into severe CAP (ICU admission is highly probable for patients with a score of 3 or 4). The management of antimicrobial treatment is similar between the two guidelines. Even if the proportion of patients with a CORB score ≥2 was quite similar, those with a CRB 65 score ≥3 was higher in EuroDEM cohort and may helped the decision of ICU admission. Finally, all differences could be explained by the higher

frequency of comorbidities such as COPD and chronic heart disease in this population: use of diuretics, beta-2 agonists and non-invasive or mechanical ventilation. This difference of comorbidities may also explain the difference of confirmed diagnosis of LRTI at discharge for hospitalised patients between the two cohorts.

This subgroup analysis has some limitations. We did not collect microbial causal agents which would have helped us better interpret the appropriateness of antibiotic use. Likewise, we had limited data on parameters such as PaO₂, albumin or procalcitonin which would have helped

to determine severity scores as SMART-COP. Chest X-ray or computed tomography scanning results were not recorded in the EuroDEM cohort. We did not distinguish bronchitis from CAP which could have provided some more insight in the likely offending micro-organism (virus or bacteria) and allowed more detailed discussion of management. There was no external committee to confirm the main diagnosis of LRTI, and in EuroDEM cohort more than one diagnosis per patient could be included. Furthermore, we had several missing data that may have influenced the results.

	Total	AANZDEM	EuroDEM	P-value
Treatment in the ED, n (%)				
CPAP	33 (2.4), missing data <i>n</i> = 12	4 (0.6)	29 (3.8)	0.001
BiPAP	42 (3.0), missing data $n = 11$	16 (2.6)	29 (3.4)	0.382
NIV combined	75 (5.4), missing data $n = 23$	20 (3.2)	58 (7.2)	< 0.001
Mechanical ventilation	19 (1.4), missing data $n = 11$	4 (0.6)	15 (2.0)	0.037
Intravenous diuretics	176 (13.1), missing data $n = 41$	45 (7.4)	131 (17.8)	< 0.001
Intravenous vasodilators	32 (2.4), missing data $n = 49$	4 (0.7)	28 (3.8)	0.001
Intravenous inotropes/ vasopressors	14 (1.0), missing data <i>n</i> = 53	6 (1.0)	8 (1.1)	0.824
Antibiotics	907 (66.5), missing data $n = 25$	444 (72.2)	463 (61.8)	< 0.001
Inhaled beta-2 agonists	546 (40.1), missing data $n = 27$	193 (31.5)	353 (47.1)	< 0.001
Corticosteroids (intravenous or oral)	316 (23.3), missing data <i>n</i> = 31	126 (20.5)	190 (25.5)	0.029
Discharge from the ED, n (%)				
Home	377 (28.3), missing data $n = 58$	153 (24.9)	224 (31.3)	0.009
Ward	916 (67.7), missing data <i>n</i> = 35	435 (70.7)	481 (65.1)	0.027
ICU	88 (6.8), missing data $n = 96$	21 (3.4)	67 (9.9)	< 0.001
Death in ED	14 (1.0), missing data $n = 1$	6 (1.0)	8 (1.0)	0.913
In-hospital outcome, n (%)				
Mortality†	109 (8.7), missing data $n = 139$	48 (7.8)	61 (9.6)	0.252
Confirmed LRTI diagnosis for hospitalised patients, n (%)	759 (75.6)	382 (83.7)	377 (68.8)	<0.001
CRB 65 score, median (Q1–Q3)	1 (0–2), performed <i>n</i> = 1219	1 (0–2), performed <i>n</i> = 584	1 (0–2), performed <i>n</i> = 635	-
CRB 65 score 0, <i>n</i> (%)	324 (26.6)	146 (25.0)	178 (28.0)	0.212
CRB 65 score 1–2, <i>n</i> (%)	820 (67.3)	415 (71.1)	405 (63.8)	0.007
CRB 65 score \geq 3, <i>n</i> (%)	75 (6.1)	23 (3.9)	52 (8.2)	0.002
CORB score, median (Q1–Q3)	0 (0–1), performed <i>n</i> = 1093	0 (0–1), performed <i>n</i> = 472	0 (0–1), performed <i>n</i> = 621	-
CORB score <2, <i>n</i> (%)	954 (87.3)	421 (89.2)	533 (85.8)	0.098
CORB $\geq 2, n (\%)$	139 (12.7)	51 (10.8)	88 (14.2)	

TA	BLE 4.	Management	at the	ED and	outcomes
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†Data are presented as number (%). BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; LRTI, lower respiratory tract infection; NIV, non-invasive ventilation.

Conclusions

In conclusion, more patients from the European cohort presented with cardio-respiratory comorbidities, received more adjunct therapies and had a higher ICU admission rate when compared to patients from the Oceania/ SEA cohort, although mortality was similar between the cohorts.

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SC, AMK, GK, CAG, PJ, AH and SL came up with the study concept and design. RB, WSK, MK, SC, GK, SK, AH, AG, CB, CAG, VPH, FV, MC, LGC and PJ collected the data. GR, IC and SL were involved in the analvsis and interpretation of the data. GR and SL drafted the manuscript. GK, OVM, SC, MK, WSK, VPH, FV, MC, CAG, AH and AMK critically revised the manuscript for important intellectual content. WSK, JC, AMK and CL contributed statistical expertise. AMK, GK, SK and CAG obtained funding. SK provided administrative and technical support. AMK, GK, CAG and SL provided study supervision.

Competing interests

GK, SC and PJ are section editors for *Emergency Medicine Australasia*. AMK is a member of the Editorial Board of *Emergency Medicine Australasia*.

Data availability statement

Research data are not shared.

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