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ORIGINAL RESEARCH

Co-morbidities and 90-day Outcomes in Hospitalized COPD Exacerbations

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COPD exacerbations resulting in hospitalization are accompanied by high mortality and morbidity. The contribution of specific co-morbidities to acute outcomes is not known in detail: existing studies have used either administrative data or small clinical cohorts and have provided conflicting results. Identification of co-existent diseases that affect outcomes provides opportunities to address these conditions proactively and improve overall COPD care. Cases were identified prospectively on admission then underwent retrospective case note audit to collect data including co-morbidities on up to 60 unselected consecutive acute COPD admissions between March and May in each hospital participating in the 2008 UK National COPD audit. Outcomes recorded were death in hospital, length of stay, and death and readmission at 90 days after index admission. 232 hospitals collected data on 9716 patients, mean age 73, 50% male, mean FEV_1 42% predicted. Prevalence of co-morbidities were associated with increased age but better FEV_1 and ex-smoker status and with worse outcomes for all four measures. Hospital mortality risk was increased with cor pulmonale, left ventricular failure, neurological conditions and non-respiratory malignancies whilst 90 day death was also increased by lung cancer and arrhythmias. Ischaemic and other heart diseases were important factors in readmission. This study demonstrates that co-morbidities adversely affect a range of short-term patient outcomes related to acute admission to hospital with exacerbations of COPD. Recognition of relevant accompanying diseases at admission provides an opportunity for specific interventions that may improve short-term prognosis.

Keywords: Mortality, length of stay, readmissions, audit

INTRODUCTION

There is an increasing recognition of the importance of co-morbidities in the long term prognosis of COPD (1,2) and the causal link between the systemic effects of COPD and other disease processes has generated recent interest in respiratory journals (3,4). Prevalence of co-morbidities in stable COPD population groups, and impact on prognosis is now relatively well described (5).

Admissions to hospital with exacerbations of COPD are associated with high risk of death, long admission stays and high readmission rates. The influence of co-morbidities on shorter term outcomes in acutely unwell patients hospitalized for exacerbations of COPD is much less clear. Although there are a number of published studies they all have significant limitations. The larger data sets have relied upon administrative coded discharge data (6) whilst clinical studies involve small numbers of patients and have other limiting factors(7,8). In some cases only one or a narrow range of co-morbidities (9,10) has been studied, in others the patients included are very different ranging from admissions to intensive care units (ICU)(11) to composite groups combining emergency with elective admissions(6).

Unsurprisingly they have provided conflicting results from almost no impact of co-morbidity on acute outcome (8,12) to specific significant associations (9). Our own much larger clinical series in the 2003 UK National Audit programme identified multiple co-morbidities as having adverse consequences in the acute hospitalization of patients but was not sufficiently detailed to provide clear relationships between specific co-morbid diseases and outcomes (13). The 2008 UK National Audit set out to address these deficiencies collecting clinician gathered prospective data in a large patient cohort. In this article we present clinically captured data from nearly 10,000 patient admissions relating co-morbidities to in hospital and 90 day outcomes of death, length of stay and readmission rates.

METHODS

The definition of co-morbidity used in this study is as defined by Rodriguez-Roisin and Soriano (3) as 'one or more distinct disorders (or diseases) in addition to COPD,

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regardless of whether this condition is or is not directly related to COPD, and irrespective of whether it is or is not part of the spectrum of the natural history of COPD'. The 2008 UK National COPD Audit collected data on co-morbidities and outcomes in patients admitted to hospital with an exacerbation of COPD. The methodology is described in detail elsewhere (14,15) but in brief all UK acute hospital National Health Service (NHS) Trusts admitting COPD exacerbations were invited to participate in an audit of clinical care.

The audit process required prospective case ascertainment of up to 60 consecutively identified COPD admissions between March and May, to maintain consistency with previous UK audit periods, which were then subjected to a retrospective case note audit at 90 days from the index admission. Data items were entered onto a bespoke web based audit tool. The items collected related to clinical care as 'documentation of clinical status of patient', 'process of care' and 'clinical outcomes'. The following outcomes were recorded: length of stay, death as 'in hospital' or after discharge but within 90 days of admission, and readmission within 90 days of the index admission.

Clinicians were asked to record specifically 'does the patient have any other significant medical conditions?' and were asked to indicate which conditions from a specified list were recorded in the medical records. 'Significant' was defined as a condition requiring medical treatment or causing symptoms. The listed conditions were: ischaemic heart disease, left ventricular failure (LVF), corpulmonale, lung cancer, cardiac arrhythmia, e.g., atrial fibrillation (AF), locomotor problems (including peripheral vascular disease, arthritis and amputation), stroke, diabetes, visual impairment, neurological condition, alcohol-related condition, psychiatric condition, other malignant disease, thromboembolic disease—pulmonary embolism or deep vein thrombosis (DVT), other cardiovascular disease, other gastrointestinal condition, and other endocrine disorder.

Missing data levels were low and reflected in this paper by variations in denominator. Within Tables 3 to 6, a series of binary regressions (STATA binreg procedure) were run to assess the association of each medical condition with outcome and to assess the association of the number of conditions (categorised as 0, 1, 2, 3 or more) with outcome; P values and confidence intervals adjusted for possible hospital clustering effects were obtained from each regression. Overall, study statistical significance was regarded as $p < 0.01$ to compensate for the large number of statistical tests performed.

Ethics approval was given by the University College Hospital/ University College London Multi-Centre Research Ethics Committee (06/Q0505/21).

RESULTS

Clinical data for 9,716 patients were received from 232 hospital units within 177 of 184 (96%) of eligible acute NHS Trusts. The median number of cases contributed by units was 46, inter-quartile range (IQR) 29–58. Overall mean (SD) patient age was 73 (10) years and half (4906) were male. The mean (SD) forced expiratory volume in 1 second (FEV_1) percentage predicted was 42% (18%) for the 5199/9716 for whom it was recorded. Where indicated 98% (8681/8863) of patients were described as 'White'. Four percent (429) lived in sheltered accommodation and 5% (503) in a residential home, while 90% (8784) lived alone or with someone else in a flat or house. Thirty-nine percent (3784) received some form of personal care. Median length of stay was five days, 19% (1630/8617) of discharged patients were accepted onto a supported (early) discharge scheme. In-hospital mortality was 7.7% (745/9716) and mortality within 90 days of the admission date was 13.9% (1289/9300). Thirty-four percent of discharged patients (2971/8677) were readmitted within the 90-day period.

The audit data item 'what other significant medical conditions did the patient have' was recorded for 98.9% (9608/9716) of cases. Seventy-seven percent (7439/9608) of these patients were documented as having co-morbidities listed in Table 1. Patients with more medical conditions were older, had worse performance status and required more social support (Table 2). They also had higher reported rates of peripheral edema. There was no notable association with gender, respiratory rate at admission, or presenting symptoms. As the number of medical conditions increased so did the percentage of ex-smokers. There was an inverse relationship between the number of co-morbidities and the % predicted FEV_1 but no notable differences in regard to admission blood gas measures, serum albumin levels or pH, but blood urea and creatinine levels rose as the number of medical conditions increased.

Table 1. Prevalence of significant other medical conditions recorded in the patient's medical records

		% (of 9608)*	Patients with condition
Ischemic Heart Disease		25.4	2439
Other cardiovascular disease		19.4	1862
Diabetes		11.8	1130
Locomotor problems		11.3	1090
Cardiac arrhythmia e.g. AF		10.0	961
Other gastro-intestinal condition		8.8	844
Psychiatric condition		7.4	708
Left Ventricular Failure (LVF)		6.7	645
Stroke		6.4	619
Other malignant disease		6.3	602
Neurological condition		5.5	528
Other endocrine disorder		4.9	467
Corpulmonale		3.3	319
Thromboembolic Disease—pulmonary embolism, DVT		3.3	313
Alcohol-related condition		2.6	250
Visual impairment		2.3	218
Lung cancer		1.9	180
Number of conditions	0	22.6	2169
	1	32.4	3117
	2	25.6	2457
	3–8	19.4	1865

*Presence or otherwise of other medical conditions in patient notes was known for 9608 of the 9716 patients.

Table 2. Patient characteristics at admission and number of significant other medical conditions recorded in the patient's medical records

	Number of significant medical conditions							
	None (N = 2169)		One (N = 3117)		Two (N = 2457)		≥Three (N = 1865)	
	%	N	%	N	%	N	%	N
Male	49	1059	50	1559	52	1265	52	976
Aged <65	31	673	23	715	18	442	14	268
Aged 65–74	34	739	31	977	29	709	27	504
Aged 75–84	28	597	34	1075	38	945	41	772
Aged 85+	7	160	11	350	15	361	17	321
Performance status:								
Normal activity	13	254/1955	10	280/2781	7	165/2220	6	97/1711
Strenuous activity limited	19	363/1955	16	451/2781	14	304/2220	11	191/1711
Limited activity but self-care	47	928/1955	48	1335/2781	50	1101/2220	47	804/1711
Limited self-care	17	339/1955	20	546/2781	22	484/2220	26	449/1711
Bed/chair bound – no self care	4	71/1955	6	169/2781	7	166/2220	10	170/1711
Paid or unpaid care	29	615/2142	37	1144/3088	43	1040/2415	51	937/1837
Current smoker	38	789/2071	34	992/2912	32	728/2302	29	506/1741
Ex-smoker	60	1245/2071	63	1826/2912	65	1490/2302	68	1182/1741
Life-long non-smoker	2	37/2071	3	94/2912	4	84/2302	3	53/1741
<20 pack years	8	90/1189	7	114/1550	8	95/1180	10	88/884
20–39 pack years	30	355/1189	29	451/1550	31	361/1180	26	227/884
40+ pack years	63	744/1189	64	985/1550	61	724/1180	64	569/884
Sputum volume increase	66	1161/1756	66	1647/2477	65	1248/1925	65	927/1420
Sputum colour change	61	1106/1803	60	1527/2525	62	1218/1980	60	878/1462
Increased breathlessness	98	2086/2132	97	2971/3051	98	2368/2423	97	1779/1827
Peripheral Edema	21	328/1590	28	641/2319	35	648/1833	46	674/1481
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age (n = 9608)	73	63–78	73	65–80	75	68–82	77	69–82
Respiratory rate (n = 8948)	24	20–28	24	20–28	24	20–28	24	20–28
FEV_1 (n = 5316)	0.80	0.51–1.06 N = 1291	0.84	0.63–1.20 N = 1717	0.91	0.66–1.24 N = 1312	0.91	0.70–1.26 N = 996
FEV_1%predicted (n = 5222)	31	22–47	38	28–50	40	30–54	41	30–56
Serum albumin g/dl (n = 7072)	40	36–42	39	35–42	38	35–41	38	34–41
Blood Urea mmol/l (n = 8845)	5.4	4.1–7.2	6.1	4.4–8.2	6.6	4.8–9.1	7.4	5.2–10.3
Blood Creatinine (n = 9199)	78	64–93	81	66–101	86	70–109	93	74–122
pH (n = 8124)	7.40	7.35–7.44	7.41	7.36–7.45	7.41	7.36–7.45	7.41	7.36–7.45
BIC mmol/l (n = 7743)	26	24–29	26	24–30	26	24–30	26	24–30
PCO_2 kPa (n = 8138)	5.9	5.0–7.3	5.8	4.9–7.2	5.7	4.9–7.1	5.7	4.9–7.1
mmHg	44.3	37.5–54.8	43.5	36.8–54.0	42.8	36.8–53.3	42.8	36.8–53.3
PO_2 kPa (n = 8140)	8.8	7.5–11.3	8.9	7.5–11.3	9.1	7.6–11.4	8.9	7.6–11.1
mmHg	66.0	56.3–84.8	66.8	56.3–84.8	68.3	57.0–85.5	66.8	57.0–83.3

IQR: Inter-QuartileRange.

When patients without a recorded FEV_1 were compared with those that had a record the prevalence of co-morbidities was similar in the two groups for most conditions, e.g., thromboembolic disease 3.3% with FEV_1 vs. 3.2% no FEV_1, cor pulmonale 3.5% with and 3.1% without, and similar results for other conditions with the exceptions of ischemic heart disease 24.4% with and 26.7% without ($p = 0.01$) and LVF 6.1% with and 7.5% without ($p = 0.006$).

Co-morbidities were associated with worse outcome in terms of in-patient mortality (Table 3), mortality within 90 days of index admission (Table 4), length of stay (Table 5), and readmission rate within 90 days of index admission (Table 6). The conditions most associated with poorer outcome in this study population were cor pulmonale, left ventricular failure, cardiac arrhythmia, neurological condition, malignant disease (either lung cancer or other malignancies), ischaemic heart disease, stroke and thromboembolic disease. The number of medical conditions was progressively predictive of mortality, length of stay of at least a week and of readmission, with patients having three or more co-morbidities being at highest risk.

Three-quarters (75%) of deaths with known cause (838/1114) were said to have been as a result of COPD or of a complication of COPD. For those with specific co-morbidities this percentage was lowest for lung cancer (47%, 23/49), thromboembolic disease (55%, 16/29) and other malignant disease (61%, 59/96). Percentages for the other specified co-morbidites ranged from 68% to 83%.

DISCUSSION

We have described in detail clinician recorded data on the prevalence and effect on 90 day outcomes of a wide range

Table 3. Co-morbidity and in-patient mortality

		% died	Patients	Risk ratio*	95% CI for risk ratio*	P-Value*
		7.6	734/9608			
Cor pulmonale		17.9	57/319	2.45	1.93–3.11	<0.001
Left Ventricular failure (LVF)		12.7	82/645	1.75	1.41–2.16	<0.001
Other malignant disease		12.1	73/602	1.65	1.32–2.06	<0.001
Neurological condition		11.7	62/528	1.59	1.24–2.03	<0.001
Lung cancer		11.1	20/180	1.47	0.96–2.25	0.08
Cardiac arrhythmia e.g. AF		9.7	93/961	1.31	1.05–1.62	0.02
Visual impairment		9.6	21/218	1.27	0.86–1.87	0.23
Stroke		9.5	59/619	1.27	0.99–1.62	0.06
Psychiatric condition		8.3	59/708	1.10	0.86–1.41	0.45
Locomotor problems		7.9	86/1090	1.04	0.84–1.28	0.73
Ischemic Heart Disease		7.5	184/2439	0.98	0.83–1.16	0.84
Other cardiovascular disease		7.3	136/1862	0.95	0.80–1.12	0.52
Diabetes		6.9	78/1130	0.89	0.70–1.14	0.36
Other gastro-intestinal condition		6.6	56/844	0.86	0.66–1.11	0.24
Other endocrine disorder		6.2	29/467	0.81	0.57–1.14	0.23
Thromboembolic Disease—pulmonary embolism, DVT		6.1	19/313	0.79	0.50–1.25	0.32
Alcohol-related condition		6.0	15/250	0.78	0.49–1.25	0.30
Number of conditions**	0	5.9	127/2169	reference	reference	reference
	1	7.8	244/3117	1.34	1.08–1.65	0.007
	2	7.9	195/2457	1.36	1.09–1.68	0.006
	3–8	9.0	168/1865	1.54	1.23–1.92	<0.001

*Risk ratios are given relative to cases without the specified co-morbidity.
**Where number of conditions = 0 this is the reference population.

of co-morbid conditions in a large cohort of COPD patients identified prospectively when admitted to hospital with exacerbations. These patients exhibit a high number of co-morbidities and this study confirms an adverse impact upon survival, length of stay and readmission over a 90-day follow-up period. It is also evident that not all co-morbidities affect the same outcomes in the same way and moreover that some co-morbid conditions affect some outcomes but not others. Increase in hospital risk of death was observed in patients with cor pulmonale, left ventricular failure, neurological conditions and non-respiratory malignancies (Table 3). At 90 days, lung cancer and cardiac arrhythmias were additional conditions with an increased risk of death.

Table 4. Co-morbidity and 90-day mortality

		% died	Patients**	Risk ratio*	95% CI for risk ratio*	P-Value*
All Cases		13.8	1272/9201			
Lung cancer		31.5	53/168	2.34	1.86–2.94	<0.001
Cor pulmonale		30.0	93/310	2.26	1.92–2.66	<0.001
Left Ventricular failure (LVF)		21.4	131/612	1.61	1.37–1.89	<0.001
Neurological condition		20.8	105/504	1.55	1.30–1.86	<0.001
Other malignant disease		19.6	113/578	1.45	1.20–1.76	<0.001
Visual impairment		18.7	39/209	1.36	1.05–1.76	0.02
Cardiac arrhythmia, e.g., AF		18.0	165/915	1.35	1.17–1.55	<0.001
Stroke		17.0	101/594	1.25	1.03–1.51	0.02
Locomotor problems		14.3	149/1045	1.04	0.88–1.22	0.67
Psychiatric condition		14.3	95/665	1.04	0.85–1.26	0.73
Other gastro-intestinal condition		14.0	113/809	1.01	0.84–1.21	0.90
Alcohol-related condition		13.5	32/237	0.98	0.73–1.30	0.87
Ischemic Heart Disease		13.4	314/2338	0.96	0.85–1.08	0.53
Other cardiovascular disease		13.0	232/1791	0.92	0.81–1.05	0.24
Diabetes		12.7	136/1075	0.90	0.76–1.08	0.26
Thromboembolic Disease—pulmonary embolism, DVT		11.3	34/300	0.81	0.58–1.15	0.24
Other endocrine disorder		10.8	48/446	0.77	0.60–0.99	0.04
Number of conditions***	0	10.2	212/2081	reference	reference	reference
	1	14.5	433/2985	1.42	1.21–1.68	<0.001
	2	14.2	335/2356	1.40	1.18–1.65	<0.001
	3–8	16.4	292/1779	1.61	1.36–1.91	<0.001

*Risk ratios are given relative to cases without the specified co-morbidity.
**90-day mortality was not known for 407 patients.
***Where number of conditions = 0 this is the reference population.

Table 5. Co-morbidity and length of stay (LOS)

		Median LOS	Mean LOS	% LOS of 7 or more days	Discharged Patients	Risk ratio*	95% CI for risk ratio*	P-Value*
All Cases		5	8.87	42	3695/8869			
Cor pulmonale		7	11.45	60	157/262	1.46	1.30–1.64	<0.001
Visual impairment		5	11.20	43	84/197	1.02	0.87–1.20	0.77
Stroke		7	10.53	50	280/560	1.22	1.12–1.32	<0.001
Left Ventricular Failure (LVF)		7	10.42	51	289/562	1.25	1.15–1.36	<0.001
Cardiac arrhythmia e.g. AF		7	10.32	51	445/867	1.26	1.17–1.36	<0.001
Other malignant disease		6	9.64	48	252/528	1.16	1.06–1.27	0.002
Thromboembolic Disease		7	9.44	50	147/294	1.21	1.09–1.34	<0.001
Neurological condition		6	9.34	44	204/465	1.06	0.94–1.18	0.34
Locomotor problems		6	9.06	45	450/1003	1.09	1.01–1.17	0.03
Diabetes		5	8.99	43	447/1050	1.02	0.95–1.10	0.52
Other cardiovascular disease		5	8.91	43	736/1725	1.03	0.96–1.10	0.40
Alcohol-related condition		6	8.86	43	101/235	1.03	0.89–1.20	0.68
Other endocrine disorder		6	8.75	43	188/438	1.03	0.92–1.16	0.59
Psychiatric condition		5	8.58	42	271/649	1.00	0.91–1.11	0.96
Ischemic Heart Disease		5	8.57	42	952/2253	1.02	0.96–1.08	0.54
Lung cancer		6	8.41	41	66/160	0.99	0.82–1.19	0.91
Other gastro-intestinal condition		5	8.36	40	316/787	0.96	0.88–1.05	0.35
Number of conditions	0	5	8.08	35	712/2040	reference	reference	reference
	1	5	8.84	41	1191/2873	1.19	1.09–1.29	<0.001
	2	6	9.05	44	997/2262	1.26	1.15–1.38	<0.001
	3–8	6	9.62	47	795/1694	1.34	1.23–1.47	<0.001

*Risk ratios (for LOS of at least 7 days) are given relative to cases without the specified co-morbidity.
Where number of conditions = 0 this is the reference population.

The findings of this study of exacerbations demonstrates contrasts with longer term epidemiological studies where other conditions are have much greater influence on mortality. For example, diabetes, where there is evidence to support this as a significant risk factor in both stable (2) and exacerbating COPD (10) and ischaemic heart disease, do not appear to have an early mortality significance in the acute COPD exacerbation (16,17). The current study makes distinctions between the categories of heart disease and in this acute situation suggests that heart failure and rhythm disturbances are important in determining both in hospital and 90-day mortality.

However, most deaths are caused by COPD or the complications of COPD, e.g., cor pulmonale, a finding consistent with studies of medium- term outcomes in ventilated COPD patients (18,19). The likely explanation for this difference in

Table 6. Co-morbidity and 90 day re-admission (since index admission) for discharged patients

		% Re-admitted	Discharged Patients	Risk ratio*	95% CI for risk ratio*	P-Value*
All Cases		34	2937/8586			
Cor pulmonale		46	117/257	1.34	1.18–1.54	<0.001
Lung cancer		44	69/156	1.30	1.08–1.56	0.005
Neurological condition		42	187/450	1.23	1.09–1.39	0.001
Left Ventricular Failure (LVF)		41	222/539	1.22	1.10–1.35	<0.001
Alcohol-related condition		41	93/229	1.19	1.02–1.40	0.03
Ischemic Heart Disease		39	849/2179	1.20	1.12–1.27	<0.001
Cardiac arrhythmia, e.g., AF		37	310/841	1.09	0.99–1.19	0.08
Diabetes		37	381/1019	1.11	1.01–1.21	0.02
Psychiatric condition		37	228/624	1.07	0.96–1.20	0.22
Thrombo-embolic Disease		37	104/282	1.08	0.90–1.30	0.40
Locomotor problems		36	349/976	1.05	0.96–1.15	0.28
Stroke		36	196/537	1.07	0.95–1.20	0.24
Other gastro-intestinal condition		35	266/766	1.02	0.93–1.12	0.73
Visual impairment		33	64/193	0.97	0.80–1.18	0.75
Other malignant disease		33	170/514	0.96	0.85–1.10	0.60
Other cardiovascular disease		32	529/1676	0.91	0.84–0.98	0.01
Other endocrine disorder		32	135/425	0.93	0.81–1.06	0.27
Number of conditions	0	30	596/1977	reference	reference	reference
	1	34	938/2775	1.12	1.02–1.23	0.02
	2	36	779/2189	1.18	1.08–1.29	<0.001
	3–8	38	624/1645	1.26	1.14–1.39	<0.001

*Risk ratios are given relative to cases without the specified co-morbidity.
Where number of conditions = 0 this is the reference population.

acute and longer-term studies is that patients admitted with COPD exacerbations have their immediate prognosis determined more by the primary reasons for admission, specifically the severity of the exacerbation, than by a co-morbid disease (20).

Although longer-term epidemiological study cohorts characterized by predominantly milder COPD subjects demonstrate an excess of non-respiratory deaths, shorter cohort studies of more severe patients have produced conflicting data with both respiratory and non-respiratory causes of death reported (21,22). The explanation for this apparent contradiction may again be found in the patient group in that stable COPD patients, even severe ones, are at greater risk to succumb to co-morbidities than similar COPD patients who are exacerbating.

Similar findings of high levels of death attributable directly to COPD were also found in the 2003 UK National COPD Audit of acute hospitalized patients but it is important to note that the proportion of deaths not attributable to COPD increased between the audit periods from 19% to 25% (13). This may be because serious co-morbid medical conditions become relatively more important as the treatment of acute COPD improves with for example the introduction of potentially life-extending, non-invasive ventilation applied to 11% of admissions in this audit (23).

Deaths related to malignant disease are also prevalent in these patients. While there may be no surprise at the increased risk of death in patients with both lung cancer and non-respiratory malignancies the combination of known malignant disease and a hospital admission with COPD is notable because of the short-term subsequent risk of death. The admission of such a patient should at least trigger a re-evaluation of palliative care support and consideration to proactively introduce end of life care pathways.

Patients with more medical conditions had higher levels of FEV_1 reported both in absolute terms and as a percentage predicted. This may be a result of a systematic recording bias, i.e., co-morbid conditions are less likely to be recorded in severe COPD patients. Such a hypothesis has been suggested on evidence derived from discharge diagnoses (3,4), but there is no reason to suspect clinician recording bias within case note entries. Alternatively the apparent reduction in co-morbidities within the severe COPD group may be explained by either a survival phenomenon, i.e., the severe COPD patients with other severe co-morbidities do not survive leaving only the severe COPD patients without co-morbidity, or by an increased likelihood that patients with moderate COPD and severe co-morbidities are more likely to be admitted by emergency physicians because of their co-morbidities.

It is also clear that patients with multiple co-morbidities have similarly abnormal blood gas measures but neither more severe respiratory nor metabolic status at admission than those with fewer co-morbidities (Table 2). The other outcome measures in this study were also affected by co-morbidities but not always by the same medical conditions as affect mortality. Both stroke and thromboembolic disease in addition to corpulmonale, LVF and arrhythmias were linked to increased length of stay (Table 5) whilst readmissions were increased in those with cardiac disease, both LVF and ischemic heart disease, and with cor pulmonale (Table 6). In the instances of readmission rates and length of stay there was also a strong relationship between the number of co-morbidities and the adverse risk but no clear relationship for the numbers of co-morbidities and mortality unlike that observed in longer term studies following hospital admission (7,24,25).

It is clear that co-morbidity was associated with age and performance status, and we have previously demonstrated that both age and performance status are themselves strong predictors of outcome (26,27). Clinically, however there is little that one can do about age or in most cases performance status, but optimal management of co-morbid factors may be important in determining outcome, and the level of co-morbidities in older patients is likely to account in some part for their adverse outcomes. Other data suggests that co-morbid conditions in stable COPD may be under appreciated and undertreated by both patients and doctors (28).

An early appreciation of the presence of relevant co-morbidities in the acute setting requires the responsible physician to address the patient from a more holistic perspective and challenges both the concept of mono specialty care and management guidelines that focus on a single disease pathway rather than a patient with multiple medical conditions.

This study does have several design limitations that must be accounted for. It is an observational study based upon audit and not a prospective controlled study and the recording of the prevalence of co-morbidities may be so influenced. Rates are however broadly in line with those found in other studies (1,29,30), although there are no existing studies of such a large prospectively followed acute population. The reliability of diagnostic coding when recorded by two different auditors is less than might be expected for cor pulmonale. The clinical distinction made here between cor pulmonale and left ventricular failure has previously been highlighted in studies of COPD co-morbidities as an area of potential diagnostic and clinical coding confusion (3).

Although we have also found this both diagnostic labels in this study are associated with similar poor prognoses. It is also the case that some patients whose discharge diagnosis was COPD may not have had this diagnosis made on admission and so are excluded from this audit. Although some studies based upon administrative coding have found this to be a major problem, in this audit clinicians were responsible for screening all admission diagnoses and it is less likely that large numbers of undiagnosed COPD patients were omitted in this audit. It is the case, however, that only just over half the patients included had confirmatory spirometry performed and it is possible that despite a senior physician made diagnosis of COPD on clinical grounds some of these patients may not, in fact, have had COPD and may have introduced bias into the study.

It might also be argued that patients without a recorded FEV_1 are more likely to have a co-morbid condition that

produced symptoms causing admission. In our cohort this was not the case for the vast majority of conditions and whilst both ischemic heart disease and LVF did have a statistically significant bias in favor of patients with no FEV_1 recorded the significance was primarily a result of the large subject numbers and the absolute differences were small (1.4–2.3%). We conclude that in this large national group of unselected COPD patients admitted to hospital with an exacerbation there is a high prevalence of co-morbid medical conditions.

In general, co-morbidities are associated with worse outcomes related to death, length of stay and readmission rates. There are, however, a wide range of co-morbid diseases that have different correlations with the different outcomes recorded in this study. Patients with co-morbidities are admitted to hospital with milder COPD measured by FEV_1. It seems logical that greater attention given to co-morbid diseases may result in reduced admissions or readmissions and fewer deaths in the acute episode.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Ferrer M, Alonso J, Morera J, et al. Chronic obstructive pulmonary disease stage and health-related quality of life.The Quality of Life Chronic Obstructive Pulmonary Disease Group. Ann Int Med 1997; 127:1072–1079.
2. Mannino DM, Thorn D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension, and cardiovascular disease in chronic obstructive pulmonary disease. Eur Respir J 2008; 32:962–269.
3. Rodriguez-Roisin R, Soriano JB. Chronic Obstructive Pulmonary Disease with Lung cancer and/or Cardiovascular Disease. Proc Am Thorac Soc 2008; 5:842–847.
4. Barnes PJ, Celli BR. Systemic manifestations and co-morbidities of COPD. Eur Respir J 2009; 33:1165–1185.
5. Terzano C, Conti V, Di Stefano F, et al. Co-morbidity, hospitalization, and mortality in COPD: Results from a longitudinal study. Lung 2010; 188:321–329.
6. Patil SP, Krishnan JA, Lechtzin N, Diette GB. In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. Arch Int Med 2003; 163:1180–1186.
7. Groenewegen KH, Schols AM, Wouters EF. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. Chest 2007; 132:1748–1755.
8. Dewars NA, Rafique S, Kanwar B, et al. Acute exacerbations of COPD factors associated with poor treatment outcome. Chest 2000; 117:662–671.
9. Bustamante-Fermosel A, De Miguel-Yanes JM, Dufort-Falco M, Munoz J. Mortality related factors after hospitalization for acute exacerbation of chronic obstructive pulmonary disease: the burden of clinical features. Am J Emerg Med 2007; 25:515–522.
10. Parappil A, Depczynski B, Collett P, Marks GB. Effect of co-morbid diabetes on length of stay and risk of death in patients admitted with acute exacerbations of COPD. Respirology 2010; 15:918–922.
11. Nevins ML, Epstein SK. Predictors of outcome for patients with COPD requiring invasive mechanical ventilation. Chest 2001; 119:1840–1849.
12. Connors AF, Dawson NV, Thomas C, et al. Outcomes following acute exacerbation of severe chronic obstructive pulmonary disease: the SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments) Am J Crit Care Med 1996; 154:959–967.
13. Price LC, Lowe D, Anstey K, Hosker HSG, Pearson MG, Roberts CM. The UK national COPD audit 2003. Impact of hospital resources and organisation of care on patient outcome following admission for acute COPD exacerbation. Thorax 2006; 61:837–842.
14. Royal College of Physicians of London, British Thoracic Society and British Lung Foundation. Report of the National Chronic Obstructive Pulmonary Disease Audit 2008: Resources and Organisation of care in Acute NHS units across the UK. http://www.rcplondon.ac.uk/clinical-standards/ceeu/Currentwork/ncrop/Pages/Resources.aspx. Date last updated: 21 December 2009. Date last accessed: 16 March 2011.
15. Royal College of Physicians of London, British Thoracic Society and British Lung Foundation. Report of the National Chronic Obstructive Pulmonary Disease Audit 2008: clinical audit of COPD exacerbations admitted to acute NHS units. http://www.rcplondon.ac.uk/clinical-standards/ceeu/Currentwork/ncrop/Pages/Resources.aspx. Date last updated: 21 December 2009. Date last accessed: 6 June 2011.
16. Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE. The effects of a smoking cessation intervention on 14.5 year mortality: a randomised clinical trial. Ann Intern Med 2005; 142:233–239.
17. Calverley PM, Anderson JA, Celli B, et al. TORCH investigators. Salmeterol and fluticasone proprionate and survival in chronic obstructive pulmonary disease. N Eng J Med 2007; 356:775–789.
18. Christensen S, Rasmussen L, Horvath-Puho E, Lenler-Petersen P, Rhode M, Johnsen SP. Arterial blood gas derangement and level of co-morbidity are not predictors of long term mortality of COPD patients treated with mechanical ventilation. Eur J Anesth 2008; 25:550–556.
19. Ai-Ping C, Lee KH, Lim TK. In-hospital and 5-year mortality of patients treated in the ICU for acute exacerbations of COPD: a retrospective study. Chest 2005; 128:518–524.
20. Ranieri P, Bianchetti A, Margiotta A, Virgillo A, Clinic EM, Trabucchi M. Predictors of 6-month mortality in elderly patients with mild Chronic Obstructive Pulmonary Disease discharged from a medical ward after acute nonacidotic exacerbation. J Am Geriatr Soc 2008; 56:909–913.
21. Celli BR, Cote CG, Martin JM, et al. The body mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Eng J Med 2004; 350:10005–10012.
22. Zielinski J, MacNee W, Wedzicha J et al. Causes of death in patients with COPD and chronic respiratory failure. Monaldi Arch Chest Dis 1997; 52:43–47.
23. Roberts CM, Stone RA, Buckingham RJ, Pursey NA, Lowe D. Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations. Thorax 2011; 66:43–48.
24. Marti S, Munoz X, Rios J, Morell F, Ferrer J. Body weight and comorbidity predict mortality in COPD patients treated with oxygen therapy. Eur Resp J 2006; 27:689–696.
25. Almagro P, Calbo E, Ochoa de Ehaguen A, et al. Mortality after hospitalization for COPD. Chest 2002;121:1441–1148.
26. Roberts CM, Lowe D, Bucknall CE, Ryland I, Kelly Y, Pearson MG. Clinical audit indicators of outcome following admission to hospital with acute exacerbation of chronic obstructive pulmonary disease. Thorax 2002; 57:137–141.

27. Connolly MJ, Lowe D, Anstey K, Hosker HSR, Pearson MG, Roberts CM. Admissions to hospital with exacerbations of chronic obstructive pulmonary disease: effect of age related factors and service organisation. Thorax 2006; 61:843–848.
28. Barr R, Celli BR, Mannino DM, et al. Co-morbidities, patient knowledge and disease management in a national sample of patients with Chronic Obstructive Pulmonary Disease. Am J Med 2009; 122:348–355.
29. Curkendall SM, DeLuise C, Jones JK, et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada cardiovascular disease in COPD patients. Ann Epidemiol 2006; 16:63–70.
30. Cristafulli E, Costi S, Luppi F, et al. Role of co-morbidities in a cohort of patients with chronic obstructive pulmonary disease undergoing pulmonary rehabilitation. Thorax 2008; 63:487–492.