69. Diagnosis and predictors of COPD exacerbation

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Late-breaking abstract: Factors associated with medication adherence in patients with COPD

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Background: Only about 50% of patients with COPD,4th leading cause of death, adhere to prescribed regimen.Non-adherence is one of the most important obstacles in achieving optimized clinical-outcome.The purpose of this study is to identify the clinical predictors of medication adherence.
Method: 51 patients with prescribed regular medication due to COPD, were included in the study. Sociodemographic (age, sex, educational level, BMI, comorbidity, number of additional drugs); COPD-related (smoking habits, duration of disease,MRC-dyspnea-score, treatment, exacerbations) and spirometry variables were recorded. Personality traits (Eysenck Personality Questionnaire), self report of medication adherence (MARS) and health related quality of life (SF-36) were evaluated.
Results: The mean-age was 63±9.2 years, 48 (94%) were male, 68.6% had low-educational level (≤8 years), mean-FEV1 was 40.4±20.9%, 58% had MRC-score of ≤3, exacerbations-per-year was 2.2±1.9. 22 of the patients had comorbid-diseases with mean number of 3.7±2.4 additional drugs and weren't correlated with MARS. Mean MARS was 20.6±4.1 and 33.3% were nonadherent. MARS was correlated neither with personality traits nor SF-36. MARS was significantly higher in patients; whom reported themselves as regular-medication-user and benefited from therapy ($p<0.001$, $p=0.03$ respectively). Patients taking nebulizer treatment found to have significantly lower MARS than patients taking LABA ($p=0.001$), which was found to be intentional.
Conclusions: We found that; neither the sociodemographic variables, personality traits nor the disease severity; but the routinization of recommended treatment and faith in the treatment are critical for optimal medication adherence in patients with COPD

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Diagnosis of COPD exacerbations on hospital admission: Results from the European COPD audit

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Background: The suspicion of COPD in acute admissions for exacerbation is based on clinical findings and supporting test results. The features of patients with suspected COPD and the results of the main diagnostic tests in 13 European countries have been evaluated.
Methodology: Prospective observational study in which all participating hospitals collected data from all COPD admissions during a 60 d period. The preliminary results of 8,664 (73.6%) completed records out of 11,765 study cases are reported.
Results: Patient characteristics: mean age 70.5±10 yrs.; 67% male; mean BMI: 26±8.9 kg/m^2, 28.5% current smokers; mean 51±37.2pack-years. Spirometry (recorded within last 6 month) in 48.2% (mean FEV1 41.9±19.2% predicted). Symptoms distribution and the availability of diagnostic tests is reflected in the figures.

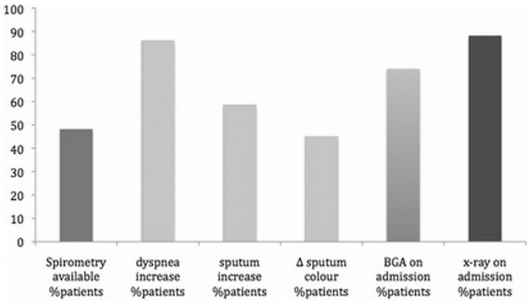

Figure 1. Mean values from 13 European countries.

The classical triad of symptoms was reported in 40.2% of the pts. BGA on admission was measured in 74% and chest-x-ray was performed in 86.6% of the pts.
Conclusion: These results help us characterise unselected COPD exacerbations as seen in clinical practice. Whilst most are admitted with dyspnea, only a minority shows the classical triad of symptoms. The high number of current smokers and the low availability of spirometry suggest to improve implementation of evidence based interventions. The severe stage of COPD in the majority of hospital admissions would justify BGA and x-ray in all patients.

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Any detectable admission cardiac troponin I level is associated with increased risk of early death following COPD exacerbations

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Background: Elevated cardiac troponin I (cTnI) levels during COPD exacerbations predict long-term mortality (COPD 2009;6:155-61). The times at which these deaths occur is unknown. We used a time-to-event approach to further characterise the prognostic significance of this biomarker.
Methods: 237 COPD patients (127 male, 73±11yrs) admitted with exacerbations between July 2008-9, and with a measured cTnI within 24h of admission were retrospectively identified. Clinical information was retrieved from the electronic patient record.
Results: Admission cTnI was "undetectable" (U, <0.02μg/L) in 15%, "measurable" (M, 0.02-0.05μg/L) in 59% and "elevated" (E, >0.05μg/L) in 26% of patients. The table shows mortality at various timepoints.
Figure 1 illustrates survival post-admission by initial cTnI level.

Days post-admission	Mortality* (%)			P
	U	M	E	
0-30	0	6	23	<0.001
30-360	6	19	25	0.07
360-545	3	4	3	0.90

*Non-cumulative.

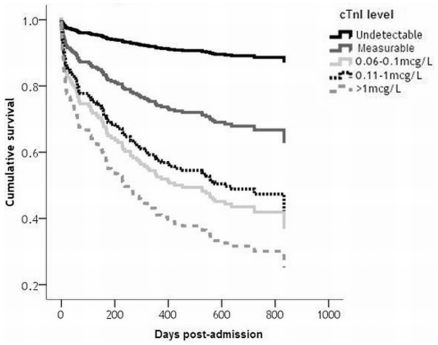

Figure 1

On Cox regression, cTnI level predicted survival (p=0.003) independently of inflammatory markers, haemoglobin, creatinine or cancer.
Conclusions: Any detectable cTnI is independently associated with increased post-exacerbation mortality, with increasing risk at higher concentrations. Excess deaths in patients with detectable cTnI occur in the first 30 days post-admission. Elucidating underlying mechanisms of cTnI rise may identify new opportunities to improve outcomes following COPD exacerbations.

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Value of prothrombin fragments F1+2 in the diagnosis of pulmonary embolism in patients hospitalized due to COPD exacerbation

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Background: One of four COPD patients who require hospitalization for an acute exacerbation may have pulmonary embolism. Normal D-dimer is now considered to be safe enough for ruling out thromboembolism in patients with a low pretest provability. However, 9% of patients with AECOPD with low clinical provability may still have PE, and D-dimer is normal only in minority of patients with AECOPD. The combining of D-Dimer testing with another markers of thrombosis may improve of the diagnostic efficiency.
Aim: To assess the usefulness of F1+2 in the diagnosis of PE in hospitalized patients with exacerbation of COPD; and whether assay of F1+2 may have an additional value in the subgroup of patients with an abnormal D- dimer. To determine the sensitivity, specificity, NPV of F1+2 at various cut off values.
Methods: Blood samples for F1+2 and D-dimer were obtained and CT pulmonary angiography was perfomed in 49 patients hospitalized due to AECOPD.
Results: Prevalence of PE was 18.37%. Patients with proved pulmonary embolism had higher values of F1+2: 380 pmol/l (95% CI 235.5 - 523.7;) than in patients with high D-dimer level in whom PE was not confirmed: 204 pmol/l (95% CI 140.2 - 268.6; p- 0.0042). At cutoff levels for F1+2 180 pmol/L or lower the sensitivity was 100%, and negative predicted value – 1,0. Taking a normal F1+2 level (cut-off 180) into account in the subgroup of patients with an abnormal D-dimer added significant clinical significance:11 of 29 patients (37.9%) could be withheld from additional imaging testing.
Conclusions: Prothrombin fragment F1+2 assay may increase the proportion of patients in whom pulmonary embolism can be safely ruled out.

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Association of the severe, frequent exacerbation phenotype with exercise capacity, sputum bacteriology and copeptin circulating levels in COPD

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Background: There is growing interest in the determinants of the frequency of exacerbation in COPD, leading to the definition of a frequent exacerbation phenotype. We have assessed variables associated with a history of frequent, severe exacerbation according to the ERS definition in a well characterized cohort of COPD patients.
Methods: Data of 598 patients with stable COPD (GOLD II-IV) for > 6 weeks, and seeking care in pulmonary tertiary hospitals in 10 European centers were analyzed. Assessment included history, systemic biomarkers (procalcitonin, proANP, copeptin, proadrenomedullin), lung function, SF-36, SGRQ, MMRC dyspnea score, and 6MWD test.
Results: Patients had a mean age of 66 yo ± 12, 448 were male. Mean FEV1% pred was 48.2% ± 18.5. A total of 387 patients (64.7%) reported no severe exacerbation, 170 (28.4%) reported one severe exacerbation, and 41 (6.9%) patients reported two or more severe exacerbations requiring hospitalization in previous year. ICU care was required in 45 (7.6%) of the cases. In the multivariate analysis, OR [95% CI] age 1.218 [1.043-1.422, p=0.013], positive sputum bacteriology at the stable state 8.88 [1.57-50.19, p=0.014], FEV1% pred 0.946 [0.902-0.992, p=0.021], MMRC 3.240 [1.021-10.281, p=0.046], 6MWD 1.014 [1.002-1.026, p=0.026], Borg 1.607 [1.010-2.558, p=0.045], and copeptin 0.305 [0.140-0.664, p=0.003] were independently associated with the severe, recurrent exacerbations phenotype.
Conclusions: Age, sputum bacteriology, lung function, dyspnea, exercise capacity and copeptin circulating levels are independently associated with the severe, frequent exacerbation phenotype.

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Predictors of hospitalisation and death with acute exacerbations of COPD

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Background: Acute exacerbations of COPD (AECOPD) are common causes of attendance to hospital emergency department (ED), but there are limited data on decision making about hospitalisation.
Aims: To analyse decision making for hospitalisation and predictors of death in patients attended with AECOPD in a public hospital in Australia.
Methods: All patients with a diagnosis of AECOPD attending the ED of the Royal Hobart Hospital between November 2006 and July 2008 (21 months) were reviewed. Patients who were admitted to the hospital were compared with those who were discharged home. Survival analysis was used to find predictors of death.
Results: 150 patients with 218 admissions (50% female, 42% current- and 58% ex-smokers, 24% with history of heart disease and 5% with previous history of myocardial infarction) were included in the study.
Those discharged from ED had a lower heart rate/minute than those admitted [mean (SD) 96 (17) vs. 105 (19), p<0.01] but there were no other differences. Age (HR=1.07, p<0.02), being female (HR=0.3, P<0.04) (female =0 and male=1), having a past history of myocardial infarction (HR=53.6, p<0.001), hypercapnia (HR=1.04, p<0.003) and co-presence of heart disease (HR=5.7, p<0.03) were the significant predictors of death during the period of the study.
Conclusions: Decision making for hospitalisation of patients in the ED seems largely arbitrary. Cardiac disease was the strongest predictor of death.

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Baseline characteristics of patients with frequent exacerbations in the POET-COPD™ trial

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Background: The randomized, double-blind, double-dummy, 1-year POET-COPD™ trial showed that tiotropium (18 µg qd) was superior to salmeterol (50 µg bid) in preventing moderate or severe chronic obstructive pulmonary disease (COPD) exacerbations.
Aims and objectives: An exploratory post-hoc subgroup analysis to compare baseline characteristics of frequent and infrequent exacerbators (patients experiencing ≥2 and ≤1 exacerbations during the trial, respectively).
Methods: Important inclusion criteria were age ≥40 years, postbronchodilator forced expiratory volume in 1 s (FEV_1) ≤70% predicted and ≥1 exacerbation in previous year.
Results: Baseline characteristics of the 7376 patients who were randomized and treated are shown in the table.
Conclusion: Compared with infrequent exacerbators, frequent exacerbators in POET-COPD™ were characterized at baseline by: more severe COPD; longer

	Frequent exacerbators (n=1004)	Infrequent exacerbators (n=6772)
Men, %	70.9	75.2
Age, yrs*	63 (8.8)	63 (9.0)
Body mass index*	26.4 (5.2)	26.7 (5.1)
COPD duration, y*	8.8 (6.7)	7.8 (6.6)
Smoking history, pack y*	39.4 (21.3)	38.1 (19.3)
Ex-smoker, %	58.3	50.8
Current smoker, %	41.7	49.2
Postbronchodilator FEV_1, mean L (% pred)	1.3 (47.2)	1.4 (49.6)
Postbronchodilator forced vital capacity, L*	2.7 (0.8)	2.7 (0.8)
Gold stage, %†		
II	41.4	49.8
III	49.2	41.6
IV	9.4	8.3
≥2 antibiotic courses†‡, %	38	24
≥2 systemic steroid courses†‡, %	23	11
Long-acting β_2-agonist (LABA) use, %†	61	50
Inhaled corticosteroid (ICS) use, %†	64.2	51.7

*Mean (SD); †$P<0.05$; ‡in the past year.

disease duration; increased LABA and ICS use; and more frequent antibiotic or systemic steroid courses in the past year.
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BNP is a predictor of mortality following COPD exacerbations

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Introduction: There is a scarcity of biomarkers to predict mortality following exacerbations of chronic obstructive pulmonary disease (COPD). Pro-Brain Natriuretic Peptide (pBNP) is an indicator of cardiac function, elevated pBNP levels indicate cardiac failure. We measured pBNP levels in addition to standard assessments in patients referred to our COPD admission avoidance (AA) service.
Methods: 33 patients (current or ex-smokers) referred for AA over a one year period had their pBNP levels checked. 6 were excluded from analysis (3 troponin positive, 1 too well, 1 refused hospital admission, 1 admitted for cardiac failure). In addition to pBNP levels, most patients had several other assessments of their lung function performed. Of the 27 patients, 4 died over the following 12 months. Statistical analysis was performed using Sigma Plot ™; data are mean + SEM.
Results: Patient mortality was associated with higher levels of pBNP (8564 + 1703 pg/mL non-survivors vs 1162 + 553 pg/mL survivors, p = 0.004). There were no significant differences in spirometry, MRC scores or oxygen saturations.
Only 2 patients in the mortality group had a previous diagnosis of heart failure, while 7 in the non-mortality group did. Only 2 patients in the mortality group were treated for congestive cardiac failure with diuretics. None were on ACE-inhibitors or other heart failure treatment.
Discussion: Despite the limitations of our study (small sample size, single center, relatively homogeneous population) pBNP may prove to be a powerful predictor for mortality following an exacerbation of COPD. In addition, our findings raise the question whether any element of underlying heart failure should be treated more aggressively in patients with COPD.