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440. Acute exacerbation in COPD

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Short term glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: "REDUCE*", a non-inferiority multicenter trial. (*Reduction in the Use of Corticosteroids in Exacerbated COPD; ISRCTN19646069)

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Background: The optimal dose and duration of systemic glucocorticoid therapy for acute exacerbations of COPD (AECOPD) is unknown. In this trial, we aimed to demonstrate non-inferiority of 5-days vs 14-days of systemic glucocorticoids with respect to COPD exacerbation.

Methods: Patients admitted to hospital with AECOPD were randomized to receive 40mg of prednisone-equivalent daily for either 5 or 14 days in a placebo-controlled fashion. Follow-up was 180 days. The primary endpoint was time to next exacerbation.

Results: Of 721 evaluated patients, 327 underwent randomization, and 304 completed the study. Mean age was 63.9±23.2 years; mean FEV1%predicted 31.5±14.3% and 60.8% were male. Exacerbations occurred in 36.8% and 38.4% of patients in the 5 day and 14 day treatment arms, respectively (p=0.81). Time to exacerbation did not differ between groups in the intention-to-treat and per-protocol analyses (hazard ratios for the short treatment arm, 0.92 [95%-CI, 0.64 to 1.34; p=0.67] and 0.91 [95%-CI, 0.63 to 1.32; p=0.62], respectively); nor did time to death or the combined endpoint of exacerbation and/or death, with both hazard ratios for the short treatment arm being <1 as well. With respect to the primary outcome, short treatment was not inferior to conventional treatment, since the 95%-confidence intervals did not include the predefined non-inferiority threshold of 1.515.

Conclusion: In AECOPD, 5-day treatment with systemic glucocorticoids is non-inferior to 14-day treatment with regard to re-exacerbation during 6 months of follow-up.

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Relationship between exacerbation frequency and survival post MI in COPD patients

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COPD patients are at increased risk of myocardial infarction (MI), particularly after an exacerbation. COPD patients have shorter survival after MI compared to the general population. We investigated whether COPD patients with frequent exacerbations (FE) had shorter survival post MI than patients with infrequent exacerbations (IE).

All COPD patients with a first MI between 1/1/03 and 31/12/08 as recorded in MINAP, who had no previous evidence of MI in GPRD or MINAP were included. Patients under 35, not registered with GPRD at the time of MI, or with less than 1 year of follow-up before their MI were excluded. Exacerbations were defined using pre-defined READ codes and prescription of pre-specified antibiotics and/or steroids. FE had ≥2 exacerbations in the year preceding MI and IE <2. Data were provided by the CALIBER group at UCL. The primary outcome was death after MI. Cox proportional hazards models were used to adjust for potential confounders. 1063 patients were identified with a first STEMI or NSTEMI. 111 (10.4%) FE and 952 (89.6%) IE. The unadjusted mortality rate in FE was 285.7 deaths (95%CI 222.3-367.2) per 1000 person years and in IE 152.4 deaths (95% CI 138.1-168.1) per 1000 person years. Adjusting for confounding by smoking and gender and stratifying by age, mortality was greater in FE compared to IE; HR 1.61(95%CI 1.23-2.11); p=0.001. Mortality was greater in patients who exacerbated in the 2 months preceding the MI; HR 3.88(2.70-5.56); p<0.001.

Conclusions: FE have shorter survival after a first MI than IE. There appears to be an association between timing of exacerbations, exacerbation frequency and survival after 1st MI.

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References:

- [1] Feary et al Thorax 2011.
- [2] Donaldson et al Chest 2010.

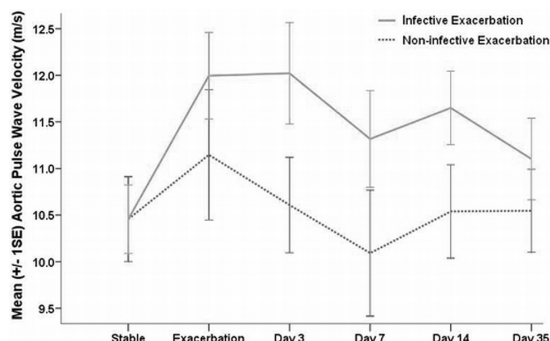
4295**The impact of airway infection on cardiovascular risk during COPD exacerbations**

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Arterial stiffness, a validated measure of cardiovascular risk, increases from stable COPD to exacerbation (Patel et al, ERS 2011). We hypothesised this increased cardiovascular risk was mediated by airway infection.

We measured aortic pulse wave velocity (aPWV) in the stable state, at exacerbation and during recovery at 3, 7, 14 and 35 days thereafter. Infective exacerbations were defined by a potentially pathogenic microbe (PPM) in exacerbation sputum by culture or positive PCR for *H. influenzae*, *S. pneumoniae*, *M. catarrhalis*, or human rhinovirus. Differences in the area under the curve (AUC) adjusted for stable aPWV level between groups were compared by unpaired t-test.

55 COPD patients (32 male, 11 current smokers) had a mean±SD FEV₁ of 1.14±0.41L (46.7±18.5%predicted) and FEV₁/FVC ratio 0.46±0.14. Two-thirds of them (36/55, 65%) produced a sputum sample at exacerbation. Two-thirds of these events (24/36, 67%) had an identifiable PPM. Patients with an infective exacerbation had a greater rise in arterial stiffness from stable state to exacerbation (1.4±1.7ms⁻¹ vs 0.4±1.0ms⁻¹, p=0.050). Arterial stiffness was also higher during the recovery period in those with an infective exacerbation (AUC 37.4±55.2ms⁻¹days vs 11.4±44.3ms⁻¹days, p=0.036).



The increase in arterial stiffness during COPD exacerbations appears to be driven by airway infection and may explain the association between these infective events and increased cardiovascular risk.

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Evaluation of multiple admissions of COPD patients: European COPD audit
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Background: Patients with multiple admissions represent an especially at risk population with therapeutic and prognostic implications. The European COPD Audit is a clinical audit to evaluate clinical practice variability, clinical and organisational factors related to outcomes for COPD admissions across Europe (422 hospitals from 13 European countries). The present communication aimed at evaluating multiple admission patients and their clinical features and outcomes.

Methods: The study comprised a first 8-week phase during which all consecutive cases admitted to hospital due to an exacerbation of COPD were identified and information on clinical practice and outcomes was gathered. During the 90-day follow-up second phase mortality and readmissions were sought. Multivariate odds ratios (OR) were calculated to evaluate factors associated with multiple admissions.

Results: Data on 14,456 cases are reported, of which 6,821 (47.2%) were the first admission (countries range 29.3-74.5%). Patients characteristics associated with multiple previous admissions were: current smoker (OR 0.69), FEV₁ value (OR 0.99), and PO₂ value (OR 1.003). Health care proved to multiple admission patients was different in terms of chest x-ray not done (OR 2.03), methylxanthines use (OR 1.2), antibiotic use (OR 0.78), diuretics use (OR 1.16) and use of NIV (OR 1.11). Reports at discharge tended to have a higher use of theophylline (OR 1.23), oxygen (OR 1.8) and mechanical ventilation (OR 1.5). We also found an impact on readmission rate (OR 0.4).

Conclusions: Multiple admission patients represent a different type of COPD patient admitted to hospital, with a more severe disease requiring more resources.

4297**Emergency oxygen use and monitoring in the pre-hospital and acute hospital setting – The significance of a common problem**

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Introduction: Evidence shows that oxygen (O₂) can cause decompensated type 2 respiratory failure (T2RF) increasing morbidity and mortality in COPD patients.

Aim: To review pre-hospital and emergency hospital use of O₂ in COPD patients.

Methods: All COPD admissions in January 2011 to Worcester Royal Hospital were audited against BTS guidelines.

Results: Ambulance documentation showed no record of previous NIV or O₂ alert card. There is no box to record FiO₂ on the ambulance data form. O₂ dose (51.6%) and mask (48.4%) recordings were suboptimal. 60% of patients were given 28% venturi masks and 13.3% non-rebreather masks. 45.8% of patients were given O₂ with adequate saturations (sats). 72% of patients given O₂ had sats > 92%.

In hospital, 9.5% of clerking contained a history of prior NIV. 2/3 of patients with adequate sats were given O₂. 80% of those on O₂ had sats above 92. 36.7% of patients had O₂ prescribed with 45% having correct sats ranges. 15 patients had T2RF; 5 with sats > 92%. 3 patients met the criteria of NIV; all had sats > 92%. Mean length of stay (LOS) was 6 days longer in those who had NIV. 90.5% of discharge letters did not contain an ABG result.

Conclusions: There is still a major issue with O₂ use and monitoring in COPD patients. Patients are being given too much O₂, it is not prescribed and not being documented accurately. This causes increased morbidity and cost, evidenced by those with hyperoxia developing T2RF and longer LOS. We recommend the ambulance data form includes an FiO₂ box, O₂ prescription is mandatory, documentation is improved and discharge letters include an ABG. Doctors, nurses and paramedics should all be regularly educated in O₂ therapy.

4298**An audit of inpatient mortality and readmission rates in acute exacerbation of COPD – Exploring the role of comorbidity and inflammatory markers**

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Acute exacerbations of COPD is the cause of rising admissions and burden on resources in spite of systems to minimise inpatient stay and facilitate discharge. The system of reimbursements in the UK NHS, penalises hospitals for readmission within 30 days. Understanding the factors leading to early readmission may help to focus resources.

We audited inpatient records of 577 (female = 260) episodes in 12-months till Dec'11. Age, co-morbidities, length of stay (LoS), readmission rate, time to readmission, white cell count and C reactive protein were collected.

218 episodes with >1 admission, 47% readmissions within 30 days; and 20 inpatient deaths. Age 69 (±11) yrs men & 72 (±12) yrs women, p=0.02. The LoS = 6 (±7) days men & 7 (±10) days women, p=ns. 344 patients had >1 associated co-morbidity. Standard mortality was 35/1000 admissions.

Patients who died were older (76±8 vs 70±11 yrs, p = 0.03) had higher (WCC 26±26 vs 12±7 x10⁹/L, p <0.001; CRP 78±100 vs 44±57 g/L, p = 0.01). A higher LoS was predicted by (WCCmax Lin regr coef B 0.118, p=0.005; CRPmax B 0.114, p=0.04) and age (Spearman's rho 0.19, p<0.001). Time to readmission was not predicted by any of the above parameters.

Inpatient mortality and LoS were predictably correlated with age and raised inflammatory markers. Nearly half of the patients were readmitted within 30 days, which would lead to morbidity and a loss of revenue. Yet, none of the common factors were found to predict the 'risk of', or 'time to' readmission. Therefore, future prevention of admission strategies may need to include telemedicine, monitoring at home and frequent flyer clinics.

4299**Differences between men and women COPD admissions: Evidence from the European COPD audit**

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Introduction: Studies using administrative data from N America provide conflicting results for gender survival differences in COPD (Machado 2006, Gonzalez 2011). We used clinician collected data to look at Hospital and 90 day survival following admission with COPD exacerbation.

Method: The European audit programme collected retrospective data from clinical case notes and telephone enquiry from 15,821 patients admitted between October

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2010 and February 2011 in 13 European countries. Data was entered onto a web collection tool and analysed centrally.

Results: Women admissions were in a minority (39.1% $P<0.001$) but proportion of all admissions varied from 53% in the UK to only 14% in Spain. Women were more likely to be non-smokers than men (9.6 vs 3.4%), had lower pack year histories if smokers (23.5 vs 31.1) but were more likely to be current smokers (37.5 vs 28.3% $P<0.001$). They were less likely to have increased sputum (60.9 vs 66.6%) or coloured sputum at admission (53.5 vs 56.3% $P<0.001$) and less likely to receive steroids or antibiotics ($P<0.001$). Women had fewer co-morbidities (1.3 vs 1.7 $P<0.001$) but were more likely to die in hospital (5.5 vs 4.7% $P=0.018$) an effect carried over to 90 days (5.6 vs 6.4% $P=0.008$) but had shorter length of stay and were less likely to be readmitted if discharged successfully (32 vs 34% $P=0.004$).

Conclusions: These data suggest women exhibit different COPD characteristics and have a higher mortality when admitted to hospital.

Machado Am J Respir Crit Care Med 2006;174:524. Gonzalez Thorax 2011;66:38.

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Acute exacerbation of COPD is associated with three-fold elevation of cardiac troponin T

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Several studies have shown that elevated levels of cardiac troponin T (cTnT) in patients hospitalised for acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is associated with dismal prognosis. The aim of the present study was to compare cTnT in patients hospitalised for AECOPD with cTnT among chronic obstructive pulmonary disease (COPD) patients in stable state.

The index group (N=50) were hospitalised due to AECOPD. They had a confirmed diagnosis of COPD before admission to the hospital. The references (n=124) were recruited from a hospital for pulmonary rehabilitation. They all had COPD in a stable state. High-sensitivity cTnT was measured within the first day of admission for AECOPD. The cumulative tobacco consumption in the index group and the references was 43 and 33 pack-years, respectively. Similarly the FEV₁/FVC-ratio in the index group and the stable state was 40% and 47%, respectively.

The geometric mean of hs-cTnT in the index group was 25.8 ng/L (95% confidence interval (CI): 21.1 – 31.7) compared with 4.5 ng/L (95% CI: 3.7 – 5.5) in the reference group. Multiple linear regression analyses showed that the ratio between hs-cTnT in AECOPD-patients and the references was 3.40 (95% CI: 2.30 – 5.02) and that hs-cTnT increased 1.34-fold (95% CI: 1.16 – 1.54), 1.24-fold (95% CI: 1.07 – 1.44) and 1.14-fold (95% CI: 1.00 – 1.29) for each quartile increase in leucocyte count, age and creatinine, respectively. A significant univariate association between cTnT and arterial hypoxemia was also found but this association attenuated almost to a zero-effect after inclusion of relevant covariates.

AECOPD is associated with elevation of hs-cTnT compared to stable COPD.