

The **COPD Digest**

Fall/Winter 2014

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A summary of clinical abstracts related to chronic obstructive pulmonary disease. The abstracts have been selected and compiled by the editorial advisory board of COPD Canada

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The COPD Digest is published by Chronicle Information Resources Ltd. for COPD Canada. Each issue reviews recently published (PubMed) clinical abstracts with related citations.

Low-dose CT measurements of airway dimensions and emphysema associated with airflow limitation in heavy smokers: a cross sectional study.

Respir Res. 2013 Jan 28;14:11. doi: 10.1186/1465-9921-14-11.

Increased airway wall thickness (AWT) and parenchymal lung destruction both contribute to airflow limitation. Advances in computed tomography (CT) post-processing imaging allow to quantify these features. The aim of this Dutch population study is to assess the relationships between AWT, lung function, emphysema and respiratory symptoms.

METHODS:

AWT and emphysema were assessed by low-dose CT in 500 male heavy smokers, randomly selected from a lung cancer screening population. AWT was measured in each lung lobe in cross-sectionally reformatted images with an automated imaging program at locations with an internal diameter of 3.5 mm, and validated in smaller cohorts of patients. The 15th percentile method (Perc15) was used to assess the severity of emphysema. Information about respiratory symptoms and smoking behavior was collected by questionnaires and lung function by spirometry.

RESULTS:

Median AWT in airways with an internal diameter of 3.5 mm (AWT_{3.5}) was 0.57 (0.44 - 0.74) mm. Median AWT in subjects without symptoms was 0.52 (0.41-0.66) and in those with dyspnea and/or wheezing 0.65 (0.52-0.81) mm (p<0.001). In the multivariate analysis only AWT_{3.5} and emphysema independently explained 31.1% and 9.5% of the variance in FEV1% predicted, respectively, after adjustment for smoking behavior.

CONCLUSIONS:

Post processing standardization of airway wall measurements provides a reliable and useful method to assess airway wall thickness. Increased airway wall thickness contributes more to airflow limitation than emphysema in a smoking male population even after adjustment for smoking behavior.

SOURCE:

Dijkstra AE1, Postma DS, ten Hacken N, Vonk JM, Oudkerk M, van Ooijen PM, Zanen P, Mohamed Hoesein FA, van Ginneken B, Schmidt M, Groen HJ. PMID: 23356533 [PubMed - indexed for MEDLINE] PMCID: PMC3570364

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A community-based exercise programme in COPD self-management: Two years follow-up of the COPE-II study.

Respir Med. 2014 Aug 7. pii: S0954-6111(14)00275-3. doi: 10.1016/j.rmed.2014.07.016. [Epub ahead of print]

It is still unknown how best to maintain effects of exercise programmes in COPD in the long-term. We present the long-term effects of a community-based exercise programme incorporated in a self-management programme, compared to a self-management programme only in patients with COPD.

METHODS:

All included patients participated in four self-management sessions. Additionally, patients in the intervention group participated in an 11-month community-based exercise programme led by physiotherapists. Patients trained three times/week for six months and two times/week during the subsequent five months. To encourage a behavioural change towards exercise, one of these weekly training sessions was home-based (unsupervised). No formal exercise training was offered to intervention patients in the second year.

RESULTS:

The intervention was assigned to 80 patients, and the control condition to 79 patients. 82.5% and 78.5% of the intervention and control group, respectively, completed 24 months follow-up. Modified intention-to-treat analyses were performed. Although statistically significant after 12 months (35.1 m (95%CI: 8.4-61.8)), the between-group difference on maximal exercise capacity was not statistically significant after 24 months (12.2 m (95%CI: -16.6 to 41.0)). Nevertheless, the between-group difference in daily physical activity was maintained after 24 months (1193 steps/day (95%CI: 203-2182)). A beneficial effect was also found on CRQ dyspnoea score but not on other CRQ domains, CCQ and HADS.

CONCLUSIONS:

Our intervention was effective in achieving a behavioural change reflected by a sustained increase in daily physical activity, not accompanied by a sustained increase in maximal exercise capacity after two years of follow-up (ISRCTN81447311).

SOURCE:

Zwerink M, van der Palen J, Kerstjens HA, van der Valk P, Brusse-Keizer M4, Zielhuis G, Effing T. PMID: 25153706

Safety and efficacy of dual bronchodilation with QVA149 in COPD patients: the ENLIGHTEN study.

Respir Med. 2013 Oct;107(10):1558-67. doi: 10.1016/j.rmed.2013.05.016. Epub 2013 Jul 16.

QVA149 is an inhaled, once-daily fixed-dose dual bronchodilator combination of the long-acting β_2 -agonist indacaterol and long-acting muscarinic antagonist glycopyrronium (NVA237) for the treatment of chronic obstructive pulmonary disease (COPD). We investigated the safety and efficacy of QVA149 over 52 weeks.

METHODS:

This 52-week, multicenter, double-blind, parallel-group, placebo-controlled study randomized (2:1) patients with moderate-to-severe COPD to once-daily QVA149 (110 µg indacaterol/50 µg glycopyrronium) or placebo delivered via the Breezhaler device. Primary endpoint was safety and tolerability for treatment-emergent adverse events (AEs). Secondary endpoints included safety based on vital signs, electrocardiograms (ECGs), laboratory evaluations, and pre-dose forced expiratory volume in 1 s (FEV1).

RESULTS:

Of 339 patients randomized, QVA149 [n = 226], placebo [n = 113]; 76.9% male, mean age: 62.6 years, post-bronchodilator FEV1: 57.4% predicted, 83.5% completed study. A smaller percentage of patients discontinued in the QVA149 group (14.2%) compared with placebo (21.2%). Overall incidence of AEs was similar in the QVA149 (57.8%) and placebo (56.6%) groups, with most AEs being mild to moderate in severity. The numerical differences in some AEs observed could be at least in part explained by differences in baseline patient characteristics. No clinically relevant differences were observed between treatment groups for vital signs or ECG parameters. The five deaths reported were unrelated to study medication (QVA149, n = 4 [1.8%]; placebo, n = 1 [0.9%]). QVA149 demonstrated rapid and clinically meaningful bronchodilation sustained over 52 weeks versus placebo.

CONCLUSIONS:

QVA149 demonstrated a good safety and tolerability profile, providing rapid and sustained bronchodilation over 52 weeks in patients with moderate-to-severe COPD.

SOURCE:

Dahl R, Chapman KR, Rudolf M, Mehta R, Kho P, Alagappan VK, Chen H, Banerji D. ClinicalTrials.gov identifier: NCT01120717. PMID: 23867808 [PubMed - indexed for MEDLINE]

Sputum-to-serum hydrogen sulfide ratio in COPD

Thorax. 2014 Jul 17. pii: thoraxjnl-2013-204868. doi: 10.1136/thoraxjnl-2013-204868. [Epub ahead of print]

Hydrogen sulfide (H₂S) is a gas produced by respiratory cells including smooth muscle cells and may play a role as a cellular gasotransmitter. We evaluated whether H₂S levels in serum or sputum could represent a new biomarker of COPD in a cross-sectional study.

METHODS:

H₂S levels in sputum and serum samples were measured using a sulfide-sensitive electrode in 64 patients with stable COPD (S-COPD), 29 COPD subjects during acute exacerbation (AE-COPD), 14 healthy smokers and 21 healthy non-smokers.

RESULTS:

Sputum H₂S levels in AE-COPD subjects were higher than those in S-COPD, healthy smoking and non-smoking subjects (p<0.001), but serum H₂S levels in AE-COPD were lower than those in S-COPD (p<0.001). Thus, the sputum-to-serum ratio of H₂S (H₂Sratio) in AE-COPD subjects were higher than those in stable COPD, healthy smoking and non-smoking subjects (p<0.001).

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In 14 COPD subjects whose H2S ratios were measured during and after an exacerbation, the mean ratio was increased during exacerbation ($p < 0.05$). H2S ratio was positively correlated with St. George's Respiratory Questionnaire score, sputum neutrophils and IL-6 and IL-8 levels in sputum and serum ($p < 0.01$) but inversely correlated with sputum macrophages (%), FEV1%predicted and FEV1/FVC ($p < 0.01$). The cut-off level of H2S ratio to indicate an exacerbation was ≥ 0.44 (sensitivity of 93.1% and specificity of 84.5%).

CONCLUSIONS:

The ratio of sputum-to-serum levels of H2S may provide a useful marker of COPD indicative of obstructive neutrophilic inflammation and of potential ongoing exacerbation.

SOURCE:

Saito J, Mackay AJ, Rossios C, Gibeon D, Macedo P, Sinharay R, Bhavsar PK, Wedzicha JA, Chung KF. PMID: 25035127 [PubMed - as supplied by publisher] [Epub ahead of print]

Comparing Cardiopulmonary Exercise Testing in Severe COPD Patients with and without Pulmonary Hypertension

Heart Lung Circ. 2014 Jan 31. pii: S1443-9506(14)00046-8. doi: 10.1016/j.hlc.2013.12.015.

To determine; (i) the effect of PH on exercise capacity, gas exchange and oxygen pulse; (ii) the variables that correlate with mean pulmonary artery pressure (mPAP) in severe COPD patients.

METHODS:

We reviewed 98 severe COPD patients who had pulmonary function, right heart catheterisation, and cardiopulmonary exercise testing (CPET) performed within six months of each other. PH was defined by a resting mPAP > 25 mmHg. COPD patients with and without PH were compared using the independent samples t-test and Mann-Whitney U test. Pearson correlation coefficients were used to assess the relationship between continuous variables.

RESULTS:

PH was present in 32% of patients and the majority of PH was mild (mPAP, 25-35mmHg). Peak workload, oxygen uptake and oxygen pulse on CPET were significantly lower in the PH group. Mean PAP was found to inversely correlate with peak oxygen uptake, with a tendency towards lower six-minute walk distance. No difference between two groups was seen in any of the gas exchange variables.

CONCLUSIONS:

In severe COPD, there is a relatively high percentage of PH which causes a decrease in exercise capacity and oxygen pulse without significantly altered ventilation as measured by CPET. Lower than expected exercise performance without a change in pulmonary function may indicate a need for evaluation for possible PH.

SOURCE:

Thirapatarapong W, Armstrong HF, Bartels MN. PMID: 24793962 PubMed - as supplied by publisher]

Evaluation of oxygen prescription in relation to hospital admission rate in patients with chronic obstructive pulmonary disease

BMC Pulm Med. 2014 Aug 5;14:127. doi: 10.1186/1471-2466-14-127.

Long term oxygen therapy (LTOT) has a strong evidence base in COPD patients with respiratory failure, but prescribing practices are recognized to need reform to ensure appropriate use and minimize costs. In the UK, since February 2006, all Home Oxygen prescription is issued by hospitals, making respiratory specialists totally in charge of home oxygen prescription. It has been widely noted that inappropriate home oxygen, often for intermittent use ("short burst"), is frequently prescribed in patients with COPD and related conditions with the intention to prevent hospital admissions outside of evidence based LTOT guidelines. We participated in a national Lung Improvement Project aimed at making LTOT use more evidence based. We utilised this unique opportunity of studying the effect of removal of oxygen from COPD patients (who did not meet LTOT criteria) on hospital admission rates.

METHODS:

Primary and secondary care data sources were used to identify patients with COPD in a single primary care trust who were admitted to hospital at least once due to COPD between April 2007 and November 2010. Admission rates were compared between LTOT users and non-users, adjusted for age and COPD severity. LTOT users were further studied for predictors of admission in those appropriately or inappropriately given oxygen according to NICE guidance, and for admissions before and after oxygen receipt, adjusting further for co-morbidity. Mortality and economic analyses were also conducted.

RESULTS:

Readmission was more likely in LTOT users (3.18 v 1.67 per patient, $p < 0.001$) after adjustment for FEV1 and age by multiple regression. When stratifying by appropriateness of LTOT prescription, adjusting also for Charlson index and other covariates, FEV1 predicted admission in appropriate users but there were no predictors in inappropriate users. In longitudinal analyses admission rates did not differ either side of oxygen prescription in appropriate or inappropriate LTOT users. Specialist assessment resulted in cost savings due to reduced use of oxygen.

CONCLUSIONS:

Admission to hospital is more likely in LTOT users, independent of COPD severity. Oxygen use outside NICE guidance does not appear to prevent admissions.

SOURCE:

Turner AM, Sen S, Steeley C, Khan Y, Sweeney P, Richards Y, Mukherjee R.
PMID: 25096821[PubMed - in process] PMCID: PMC4129429

Mortality risk prediction in COPD by a prognostic biomarker panel.

Eur Respir J. 2014 Jul 17. pii: erj00438-2014. [Epub ahead of print]

Chronic obstructive pulmonary disease (COPD) is a complex disease with various phenotypes. The simultaneous determination of multiple biomarkers reflecting different pathobiological pathways could be useful in identifying individuals with an increased risk of death.

METHODS:

We derived and validated a combination of three biomarkers (adrenomedullin, arginine vasopressin and atrial natriuretic peptide), assessed in plasma samples of 385 patients, to estimate mortality risk in stable COPD. Biomarkers were analysed in combination and defined as high or low.

RESULTS:

In the derivation cohort (n = 142), there were 73 deaths during the 5-year follow-up. Crude hazard ratios for mortality were 3.0 (95% CI 1.8-5.1) for one high biomarker, 4.8 (95% CI 2.4-9.5) for two biomarkers and 9.6 (95% CI 3.3-28.3) for three high biomarkers compared with no elevated biomarkers. In the validation cohort (n = 243), 87 individuals died. Corresponding hazard ratios were 1.9 (95% CI 1.1-3.3), 3.1 (95% CI 1.8-5.4) and 5.4 (95% CI 2.5-11.4). Multivariable adjustment for clinical variables as well as the BODE (body mass index, airflow obstruction, dyspnoea, exercise capacity) index and stratification by the Global Initiative for Chronic Obstructive Lung Disease stages provided consistent results. The addition of the panel of three biomarkers to the BODE index generated a net reclassification improvement of 57.9% (95% CI 21.7-92.4%) and 45.9% (95% CI 13.9-75.7%) at 3 and 5 years, respectively.

CONCLUSIONS:

Simultaneously elevated levels of adrenomedullin, arginine vasopressin and atrial natriuretic peptide are associated with increased risk of death in patients with stable COPD.

SOURCE:

Stolz D, Meyer A, Rakic J, Boeck L, Scherr A, Tamm M. PMID: 25034566 [PubMed - as supplied by publisher]

Symptoms and impact of symptoms on function and health in patients with chronic obstructive pulmonary disease and chronic heart failure in primary health care.

Int J Chron Obstruct Pulmon Dis. 2014 Jul 18;9:785-94. doi: 10.2147/COPD.S62563. eCollection 2014.

Patients with chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) seem to have several symptoms in common that impact health. However, methodological differences make this difficult to compare. Comparisons of symptoms, impact of symptoms on function and health between patients with COPD and CHF in primary health care (PHC).

METHODS:

The study is cross sectional, including patients with COPD (n=437) and CHF (n=388), registered in the patient administrative systems of PHC. The patients received specific questionnaires - the Memorial Symptom Assessment Scale, the Medical Research Council dyspnea scale, and the Fatigue Impact Scale - by mail and additional questions about psychological and physical health.

RESULTS:

The mean age was 70±10 years and 78±10 years for patients with COPD and CHF respectively (P=0.001). Patients with COPD (n=273) experienced more symptoms (11±7.5) than the CHF patients (n=211) (10±7.6). The most prevalent symptoms for patients with COPD were dyspnea, cough, and lack of energy. For patients with CHF, the most prevalent symptoms were dyspnea, lack of energy, and difficulty sleeping. Experience of dyspnea, cough, dry mouth, feeling irritable, worrying, and problems with sexual interest or activity were more common in patients with COPD while the experience of swelling of arms or legs was more common among patients with CHF. When controlling for background characteristics, there were no differences regarding feeling irritable, worrying, and sexual problems. There were no differences in impact of symptoms or health.

CONCLUSIONS:

Patients with COPD and CHF seem to experience similar symptoms. There were no differences in how the patients perceived their functioning according to their cardinal symptoms; dyspnea and fatigue, and health. An intervention for both groups of patients to optimize the management of symptoms and improve function is probably more relevant in PHC than focusing on separate diagnosis groups.

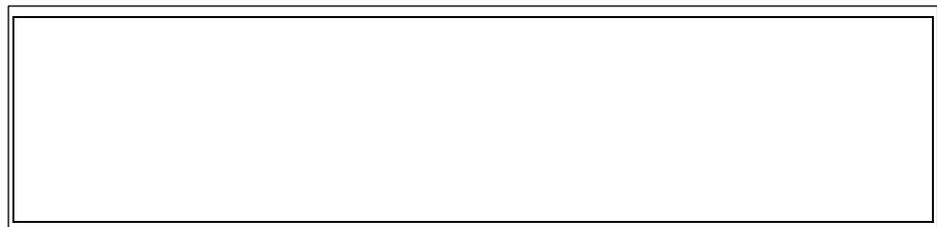
SOURCE:

Theander K, Hasselgren M, Luhr K, Eckerblad J, Unosson M, Karlsson I
PMID: 25071370 [PubMed - in process] PMID: PMC4111648

A resource for your patients:

The COPD Canada web site is your portal to our association, news and varied educational materials, medical resources and community interaction. Membership is free-of-charge but is restricted to individuals living with COPD or their caregivers. Joining is fast and easy. Just visit our web site www.copdcanada.info and click on membership, then follow the step-by-step instructions. Questions or comments should be directed to exec.copdcanada@gmail.com

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