

Contempo 2005:
Le malattie dell'anziano
Gardone Riviera (BS), 28-29/4/2005

BPCO
Raffaele Antonelli Incalzi

Riferimenti bibliografici

Respir Med. 2004 Nov;98(11):1071-9.

G

Factors determining performance of bronchodilator reversibility tests in middle-aged and elderly.

Lehmann S, Vollset SE, Nygaard HA, Gulsvik A.

Department of Thoracic Medicine, Haukeland University Hospital, University of Bergen, Bergen N-5021, Norway. sverre.lehmann@helse-bergen.no

Knowledge of the factors determining the performance of bronchodilator reversibility testing in a general population is lacking. Random samples of all adults aged 47-48 and 71-73 years living in Bergen, Norway, were invited to a cross-sectional study. Altogether 3506 subjects attended (69%). Test quality predictors were examined through multiple logistic regression analyses including gender, age, body mass, educational level, smoking history, respiratory symptoms, and in the elderly cohort cognitive level. Among the participants, 1.6% refused to inhale salbutamol, 2.5% failed the initial spirometry according to the ATS guidelines, and 1.3% failed the post-bronchodilator spirometry. Old age and body mass index > 30 kg/m² were independent risk factors for an unsuccessful initial spirometry, and never smoking and respiratory symptoms were risk factors for failing the post-bronchodilator spirometry. Cognitive impairment in the elderly was a risk factor for failing both the initial- and post-bronchodilator spirometry. The median number of forced expirations was 7 in subjects obtaining an acceptable reversibility test. One third of these participants needed > or = 8 attempts, with independent predicting factors being old age, Little formal education and never smoking. Although reversibility testing becomes increasingly difficult with age, reliable data are obtained in a vast majority (94%) of subjects in our community study.

BMJ. 2004 Nov 20;329(7476):1209. Epub 2004 Nov 20.

G

Community pulmonary rehabilitation after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study.

Man WD, Polkey MI, Donaldson N, Gray BJ, Moxham J.

Respiratory Muscle Laboratory, Guy's, King's, and St Thomas' School of Medicine, King's College Hospital, London SE5 9PJ. william.man@kcl.ac.uk

OBJECTIVE: To evaluate the effects of an early community based pulmonary

rehabilitation programme after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease (COPD). DESIGN: A single centre, randomised controlled trial. SETTING: An inner city, secondary and tertiary care hospital in London. PARTICIPANTS: 42 patients admitted with an acute exacerbation of COPD. INTERVENTION: An eight week, pulmonary rehabilitation programme for outpatients, started within 10 days of hospital discharge, or usual care. MAIN OUTCOME MEASURES: Incremental shuttle walk distance, disease specific health status (St George's respiratory questionnaire, SGRQ; chronic respiratory questionnaire, CRQ) and generic health status (medical outcomes short form 36 questionnaire, SF-36) at three months after hospital discharge. RESULTS: Early pulmonary rehabilitation, compared with usual care, led to significant improvements in median incremental shuttle walk distance (60 metres, 95% confidence interval 26.6 metres to 93.4 metres, $P = 0.0002$), mean SGRQ total score (-12.7, -5.0 to -20.3, $P = 0.002$), all four domains of the CRQ (dyspnoea 5.5, 2.0 to 9.0, $P = 0.003$; fatigue 5.3, 1.9 to 8.8, $P = 0.004$; emotion 8.7, 2.4 to 15.0, $P = 0.008$; and mastery 7.5, 4.2 to 10.7, $P < 0.001$) and the mental component score of the SF-36 (20.1, 3.3 to 36.8, $P = 0.02$). Improvements in the physical component score of the SF-36 did not reach significance (10.6, -0.3 to 21.6, $P = 0.057$). CONCLUSION: Early pulmonary rehabilitation after admission to hospital for acute exacerbations of COPD is safe and leads to statistically and clinically significant improvements in exercise capacity and health status at three months.

Respir Med. 2004 Oct;98(10):1000-7.

G

Heavy resistance training increases muscle size, strength and physical function in elderly male COPD-patients--a pilot study.

Kongsgaard M, Backer V, Jorgensen K, Kjaer M, Beyer N.

Institute of Sports Medicine, Bispebjerg Hospital, Bispebjerg Bakke 23, Copenhagen, Denmark.
mads.kongsgaard@get2net.dk

This study investigated the effects of heavy resistance training in elderly males with chronic obstructive pulmonary disease (COPD). 18 Home-dwelling male patients (age range: 65-80 years), with a mean forced expiratory volume in the first second (FEV1) of 46 +/- 3.4% of predicted value, were recruited. Baseline and post-training assessments included: Cross-sectional area (CSA) of quadriceps assessed by MRI, isometric and isokinetic knee extension strength, isometric trunk strength, leg extension power, normal and maximal gait-speed on a 30 m track, stair climbing time, number of chair stands in 30 s, lung function (FEV1) and self-reported health. Subjects were randomized to a resistance training group (RE, $n = 9$) or a control group conducting breathing exercises (CON, $n = 9$). RE performed heavy progressive resistance training twice a week for 12 weeks. 6 RE and 7 CON completed the study. In RE the following improved ($P < 0.05$): Quadriceps CSA: 4%, isometric knee extension strength: 14%, isokinetic knee extension strength at 60 degrees /s.: 18%, leg extension power: 19%, maximal gait speed: 14%, stair climbing time: 17%, isometric trunk flexion: 5% and self-reported health. In CON no changes were found. In conclusion, 12 weeks of heavy resistance training twice a week resulted in significant improvements in muscle size, knee extension strength, leg extension power, functional performance and self-reported health in elderly male COPD patients.

Proc Natl Acad Sci U S A. 2004 Oct 12;101(41):14895-900. Epub 2004 Oct 05.

Comprehensive gene expression profiles reveal pathways related to the pathogenesis of chronic obstructive pulmonary disease.

Ning W, Li CJ, Kaminski N, Feghali-Bostwick CA, Alber SM, Di YP, Otterbein SL, Song R, Hayashi S, Zhou Z, Pinsky DJ, Watkins SC, Pilewski JM, Sciruba FC, Peters DG, Hogg JC, Choi AM.

Division of Pulmonary Allergy and Critical Care Medicine, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA.

To better understand the molecular basis of chronic obstructive pulmonary disease (COPD), we used serial analysis of gene expression (SAGE) and microarray analysis to compare the gene expression patterns of lung tissues from COPD and control smokers. A total of 59,343 tags corresponding to 26,502 transcripts were sequenced in SAGE analyses. A total of 327 genes were differentially expressed (1.5-fold up- or down-regulated). Microarray analysis using the same RNA source detected 261 transcripts that were differentially expressed to a significant degree between GOLD-2 and GOLD-0 smokers. We confirmed the altered expression of a select number of genes by using real-time quantitative RT-PCR. These genes encode for transcription factors (EGR1 and FOS), growth factors or related proteins (CTGF, CYR61, CX3CL1, TGF β 1, and PDGFRA), and extracellular matrix protein (COL1A1). Immunofluorescence studies on the same lung specimens localized the expression of Egr-1, CTGF, and Cyr61 to alveolar epithelial cells, airway epithelial cells, and stromal and inflammatory cells of GOLD-2 smokers. Cigarette smoke extract induced Egr-1 protein expression and increased Egr-1 DNA-binding activity in human lung fibroblast cells. Cytomix (tumor necrosis factor alpha, IL-1beta, and IFN-gamma) treatment showed that the activity of matrix metalloproteinase-2 (MMP-2) was increased in lung fibroblasts from EGR1 control (+/+) mice but not detected in that of EGR1 null (-/-) mice, whereas MMP-9 was regulated by EGR1 in a reverse manner. Our study represents the first comprehensive analysis of gene expression on GOLD-2 versus GOLD-0 smokers and reveals previously unreported candidate genes that may serve as potential molecular targets in COPD.

J Rehabil Med. 2004 Jul;36(4):153-8.

I

Performance changes for patients with chronic obstructive pulmonary disease on long-term oxygen therapy after physiotherapy.

Faager G, Larsen FF.

Department of Physiotherapy, Karolinska Hospital, Stockholm, Sweden.
gun.faager@ks.se

OBJECTIVE: To investigate whether patients with chronic obstructive pulmonary disease on long-term oxygen therapy would benefit from an early 8-week rehabilitation programme in terms of exercise performance, health-related quality of life and activities of daily living. **METHODS:** Two weeks after onset of oxygen therapy, 20 patients were randomized to rehabilitation (group A) or not (group B). Exercise performance was measured using a 6-minute walking test. Health-related quality of life was measured with the Chronic Respiratory Disease Questionnaire. Activity of daily living ability was measured with the Stanford Health Assessment Questionnaire. **RESULTS:** The mean

6-minute walking distance increased by 35% ($p < 0.01$) in group A after rehabilitation. The mean increase in group B was only 8% (n.s.). Patients in group A reported less overall dyspnoea after rehabilitation ($p < 0.05$) and, compared with group B, reported better activity of daily living ability ($p < 0.01$). CONCLUSION: Patients with chronic obstructive pulmonary disease on long-term oxygen treatment may improve their walking distance, experience less dyspnoea and improve activity of daily living ability with an early rehabilitation programme.

Age Ageing. 2004 Nov;33(6):567-70. Epub 2004 Sep 03.

A

Length of stay and interval to readmission in emergency hospital treatment of COPD.

Saynajakangas O, Kinnunen T, Tuuponen T, Keistinen T.

Lapland Central Hospital, Department of Pulmonary Diseases, PL 8041, Fin 96101 Rovaniemi, Finland. olli.saynajakangas@fimnet.fi

BACKGROUND: increasing attention has recently been attached to the length of hospital stay and related factors in the treatment of COPD. OBJECTIVES: to assess the trend in the duration of inpatient episodes following emergency admissions for COPD by age and sex, and the frequency of readmissions, as well as the correlations between the frequency and duration of inpatient episodes. DESIGN: retrospective study. SETTING: the Finnish hospital discharge register. SUBJECTS: the 72,672 inpatient episodes following emergency admissions of patients aged over 44 years that ended in 1993-2001 and had COPD as the principal diagnosis. RESULTS: the mean duration of inpatient episodes was 8.5 days (SD 8.2) in 1993, but 6.8 days (SD 6.6) in 2001. The figure for 45- to 64-year-old men was 6.5 days (SD 6.6) and that for men aged >64 years, 7.8 days (SD 6.8). The corresponding figures for women were 7.1 days (SD 6.8) and 8.8 days (SD 8.4). The average interval between the end of one inpatient episode and the beginning of the next was 195.4 days (SD 327.7). This interval was longest when the inpatient episode lasted for 7 days (interval 215 days). CONCLUSIONS: the length of hospital stay for COPD exacerbation seems to be decreasing, and elderly women have the longest inpatient episodes. With the current treatment modalities, a 1-week stay in hospital results in the longest interval to readmission. The situation may change if supported home care at exacerbation can be increased.

J Okla State Med Assoc. 2004 Jun;97(6):227-32.

G

Management of acute exacerbations of chronic obstructive pulmonary disease in the elderly: physician practices in the community hospital setting.

Bratzler DW, Oehlert WH, McAdams LM, Leon J, Jiang H, Piatt D.

Oklahoma Foundation for Medical Quality, 14000 Quail Springs Parkway, Suite 400, Oklahoma City, OK 73134, USA. okpro.dbratzler@sdps.org

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death and sixth most common reason that Medicare patients are hospitalized. We performed

retrospective chart review on a statewide random sample of 409 Medicare patients discharged from October 1, 2000, through January 31, 2001, with a diagnosis of COPD. The most commonly performed diagnostic tests were chest radiography (96.8%) and oxygenation assessment (94.9%). The most common treatments provided were inhaled short-acting beta-agonist bronchodilators (98.5%) and oxygen (94.4%). Antibiotics (89.0%) and systemic corticosteroids (85.1%) were prescribed less frequently. The median length of stay was 5 days. The readmission rate was 27.4% (CI, 23.1-32.0) at 30 days and 43.0% (CI, 38.2-47.9) at 180 days. The in-hospital mortality rate was 1.7% (CI, 0.7-3.5) and the 180-day mortality rate was 23.7% (CI, 19.7-28.1). The morbidity and mortality associated with acute exacerbations of COPD remain high. There are opportunities to improve quality of care for this condition.

Scand J Infect Dis. 2004;36(5):330-4.

A

Comparative study of community-acquired pneumonia caused by Streptococcus pneumoniae, Legionella pneumophila or Chlamydia pneumoniae.

Sopena N, Pedro-Botet ML, Sabria M, Garcia-Pares D, Reynaga E, Garcia-Nunez M.

Infectious Diseases Unit, University Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain. nsopena@ns.hugtip.scs.es

The objective of this study was to compare epidemiological data and clinical presentation of community-acquired pneumonia (CAP) caused by Streptococcus pneumoniae, Legionella pneumophila or Chlamydia pneumoniae. From May 1994 to February 1996, 157 patients with S. pneumoniae (n = 68), L. pneumophila (n = 48) and C. pneumoniae (n = 41) pneumonia with definitive diagnosis, were prospectively studied. The following comparisons showed differences at a level of at least $p < 0.05$. Patients with S. pneumoniae pneumonia had more frequently underlying diseases (HIV infection and neoplasm) and those with C. pneumoniae pneumonia were older and had a higher frequency of chronic obstructive pulmonary disease (COPD), while L. pneumophila pneumonia prevailed in patients without comorbidity, but with alcohol intake. Presentation with cough and expectoration were significantly more frequent in patients with S. pneumoniae or C. pneumoniae pneumonia, while headache, diarrhoea and no response to betalactam antibiotics prevailed in L. pneumophila pneumonia. However, duration of symptoms $> \text{ or } = 7 \text{ d}$ was more frequent in C. pneumoniae pneumonia. Patients with CAP caused by L. pneumophila presented hyponatraemia and an increase in CK more frequently, while AST elevation prevailed in L. pneumophila and C. pneumoniae pneumonia. In conclusion, some risk factors and clinical characteristics of patients with CAP may help to broaden empirical therapy against atypical pathogens until rapid diagnostic tests are available.

Thorax. 2004 Aug;59(8):668-72.

Effect of oxygen on recovery from maximal exercise in patients with chronic obstructive pulmonary disease.

Stevenson NJ, Calverley PM.

Clinical Science Centre, University Hospital Aintree, Liverpool L9 7AL, UK.

BACKGROUND: The effects of oxygen on recovery from exercise in patients with chronic obstructive pulmonary disease (COPD) are not clearly known. A study was undertaken to determine whether oxygen given after maximal exercise reduced the degree of dynamic hyperinflation and so reduced the perception of breathlessness. **METHODS:** Eighteen patients with moderate to severe COPD performed maximal symptom limited exercise on a cycle ergometer. During recovery they received either air or oxygen at identical flow rates in a randomised, single blind, crossover design. Inspiratory capacity, breathing pattern data, dyspnoea intensity, and leg fatigue scores were collected at regular intervals during recovery. At a subsequent visit patients underwent a similar protocol but with a face mask in situ to eliminate the effects of instrumentation. **RESULTS:** When oxygen was given the time taken for resolution of dynamic hyperinflation was significantly shorter (mean difference between air and oxygen 6.61(1.65) minutes (95% CI 3.13 to 10.09), $p = 0.001$). Oxygen did not, however, reduce the perception of breathlessness during recovery nor did it affect the time taken to return to baseline dyspnoea scores in either the instrumented or non-instrumented state (mean difference 2.11 (1.41) minutes (95% CI -0.88 to 5.10), $p = 0.15$). **CONCLUSIONS:** Oxygen reduces the degree of dynamic hyperinflation during recovery from exercise but does not make patients feel less breathless than breathing air. This suggests that factors other than lung mechanics may be important during recovery from exercise, or it may reflect the cooling effect of both air and oxygen.

Respir Med. 2004 Jul;98(7):661-8.

A

Extubation failure in the elderly.
EI Solh AA, Bhat A, Gunen H, Berbarry E.

Department of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, NY 14215, USA.
solh@buffalo.edu

To determine the causes, risk factors and complications of planned extubation failure of critically ill elderly patients, we conducted a prospective study of 175 consecutive patients ($> \text{ or } = 70$ years old) admitted with respiratory failure. Thirty-six (21%) failed extubation within 72 h after planned extubation. Compared to a younger age group (< 70 years old) matched for severity of illness, inability to handle secretions (20%) was the most common reason of airway causes leading to extubation failure in the elderly while upper airway obstruction (22%) was the predominant cause in the control group. As for nonairway causes, COPD related hypercapnic respiratory failure accounted for the majority of cases in both groups. After adjusting for severity of illness, elderly patients who required reintubation had a higher risk of developing nosocomial pneumonia. The presence of underlying pulmonary disease (odds ratio (OR), 2.9; 95% confidence interval (CI) 1.2-6.9), length of intubation > 4 days (OR, 4.3; 95% CI 1.8-10.2), and albumin levels < 2.5 g/dl (OR, 2.7; 95% CI 1.2-6.7) were independently associated with extubation failure in the old. Objective measurements of cough strength and secretion volume are needed to reduce the morbidity of elderly patients at risk for extubation failure.

Chest. 2004 Jul;126(1):165-72.

A

The use of noninvasive ventilation in acute respiratory failure at a tertiary care center.

Paus-Jenssen ES, Reid JK, Cockcroft DW, Laframboise K, Ward HA.

Department of Medicine, Royal University Hospital, Saskatoon, SK, Canada.

OBJECTIVE: Financial constraints and bed limitations frequently prevent admission of ill patients to a critical care setting. We surveyed the use of treatment with noninvasive ventilation (NIV) in clinical practice by physicians in a tertiary care, university-based teaching hospital and compared our findings with published recommendations for the use of NIV. **METHODS:** Data were collected prospectively on all patients with acute respiratory failure (ARF) for whom NIV was ordered over a 5-month period. The respiratory therapy department was responsible for administering NIV on written order by a physician. The respiratory therapist completed a survey form with patient tracking data for each initiation of NIV. The investigators then surveyed the clinical chart for clinical data. **RESULTS:** NIV was utilized for the treatment of ARF on 75 occasions during the 5-month period. Fourteen patients (18%) received NIV for a COPD exacerbation, and 61 patients (82%) received it for respiratory failure of other etiologies. NIV was initiated in the emergency department in 32% of patients, in a critical care setting in 27% of patients, in a ward observation unit in 23% of patients, and on a general medical or surgical ward in 18% of patients. Arterial blood gases (ABGs) were measured on 68 occasions prior to the initiation of NIV, and 51 patients had an ABG measurement within the first 6 h of treatment. The mean pH at baseline was 7.29, and 33% of patients had a baseline pH of < 7.25. Seven patients required endotracheal intubation (ETI) [13%], and there were 18 deaths (24%) with patients having do-not-resuscitate orders, accounting for 12 deaths. **CONCLUSION:** NIV is commonly used outside of a critical care setting. Our outcomes of ETI and death were similar to those cited in the literature despite less aggressive monitoring of these patients.

Arch Gerontol Geriatr. 2004 Sep-Oct;39(2):111-6.

G

Pneumonia in elderly patients with preexisting respiratory disease.

Sumi M, Satoh H, Ishikawa H, Sekizawa K.

Division of Respiratory Medicine, Institute of Clinical Medicine, University of Tsukuba, Tsukuba-city, Ibaraki 305-8575, Japan.

To evaluate the optimal duration of appropriate antibiotic therapy for pneumonia in elderly patients with preexisting respiratory disease, we studied improvement of infectious parameters in these patients. The medical record database was used to identify patients admitted with the following characteristics: primary diagnosis of benign respiratory disease; aged 65 years or over; no active malignant diseases in any organs; and at least one admission for pneumonia during April 2001 to May 2003. We observed 47 pneumonia episodes in 30 patients. Elevated CRP levels more than 8.0 mg/ml and leukocytosis more than 10.0×10^3 mm⁻³ was seen in 21 and 29 pneumonia episodes, respectively. With appropriate intravenous antimicrobial therapy, average of CRP levels on day 0 (9.16 +/- 6.81 mg/dl) decreased to 5.18 +/- 4.67 mg/dl on day 3 (P = 0.0073). In more than 70% of pneumonia episodes, serum levels of CRP normalized on day 10. Average of leukocyte counts on day 0 ($(12.3 \pm 4.7) \times 10^3$)

mm(-3)) decreased to (8.1 +/- 3.5) x 10(3) mm(-3) on day 3 (P = 0.0001). In more than 80% of pneumonia episodes, leukocyte count normalized on day 7. The clinical response to appropriate antimicrobial therapy for pneumonia occurs within the first 3 days of therapy. Duration of intravenous antimicrobial therapy for pneumonia in these patients of 10 days would be sufficient and could prevent recurrent infection with resistant bacteria.

Emerg Med Australas. 2004 Jun;16(3):212-5.

G

Elevation of cardiac troponins in exacerbation of chronic obstructive pulmonary disease.

Harvey MG, Hancox RJ.

Emergency Department, Monash Medical Centre, Melbourne, Victoria, Australia.
martyinandcait@optusnet.com.au

OBJECTIVES: To investigate the prevalence of serum troponin elevation in patients admitted to hospital with an exacerbation of chronic obstructive pulmonary disease (COPD). **METHODS:** We examined the records of all patients admitted to hospital for treatment of COPD for serum troponin measurement, clinical features of myocardial ischaemia, oxygenation (pulse oximetry, arterial blood gas analysis), spirometry, and duration of admission. **RESULTS:** Troponin elevation was observed in 58 of 235 (25%) presentations in which troponin was measured. Despite the troponin result, only seven of these 58 patients had been diagnosed with an acute coronary syndrome. New ECG evidence of ischaemia was uncommon. Patients with raised troponins tended to be older (75.7 vs 70.0 years, P = 0.001), had lower pulse oximetry (85.6% vs 89.6%, P = 0.003), were more acidotic (pH 7.34 vs 7.40, P = 0.002) and more hypercapnoeic (pCO₂ 58.0 vs 49.1, P = 0.04). There were no significant differences in serum creatine kinase. Patients with raised troponins had significantly longer admissions (5 vs 3 days, P = 0.001). **CONCLUSIONS:** Serum troponins are commonly raised in acute exacerbations of COPD and appear to reflect the severity of the exacerbation. In the majority of patients there is insufficient evidence to support the diagnosis of an acute coronar

J Med Assoc Thai. 2004 Apr;87(4):377-81.

G

Prevalence and incidence of Chlamydia pneumoniae antibodies among the healthy elderly and patients with chronic obstructive pulmonary diseases.

Siritantikorn S, Maranetra KN, Wongsurakiat P, Praditsuwan R, Puthavathana P, Ngamurult S, Suthamsamai T.

Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Chlamydia pneumoniae is an obligatory intracellular bacteria which can cause both acute and chronic respiratory tract infection. The significance of chronic and recurrent respiratory infection may be of prime importance in chronic obstructive pulmonary diseases (COPD). The purpose of this study was to determine the prevalence and incidence of C. pneumoniae antibodies in elderly COPD patients compared to a

healthy elderly control group. C. pneumoniae antibodies were detected by an enzyme-linked immunosorbent assay in serum samples obtained from 127 elderly COPD patients and a 131 healthy elderly control group. The results showed that the seroprevalence of C. pneumoniae infection as determined by the existence of specific IgG or IgA or IgM antibodies was 96.1% in the COPD patients and 75.6% in the control group ($p < 0.01$). The prevalence of individual C. pneumoniae IgG, IgA and IgM in elderly COPD vs healthy control was 85.8% vs 66.4%, 85.0% vs 51.1% and 3.9% vs 0%, respectively. The incidence or seroconversion rate of C. pneumoniae antibodies after one year follow-up was found to be 33% in the COPD patients and 67.9% in the control group. High prevalence and incidence of C. pneumoniae antibodies indicates that both acute and chronic C. pneumoniae infection play a role in elderly COPD patients. Therefore, antibiotics of choice for C. pneumoniae infection should probably be considered.

Disabil Rehabil. 2004 Jun 3;26(11):641-8.

I

Evaluation of patients with severe pulmonary disease before and after pulmonary rehabilitation.

Goldberg R, Hillberg R, Reinecker L, Goldstein R.

Department of Psychiatry, Spaulding Rehabilitation Hospital, Harvard Medical School
Boston, MA 02114, USA.

PURPOSE: The purpose was to evaluate the impact of inpatient pulmonary rehabilitation program upon changes in anxiety, depression, psychological outlook, and dyspnea. A secondary purpose was to predict changes in psychological outlook, depression, anxiety, and dyspnea by using three pulmonary function tests and age. **METHODS:** The design consisted of an observational study with pre-post comparisons. Forty-five patients with severe pulmonary disease, mean age 67.4 years (SD 9.2), mean FEV(1)=31.44% predicted, 13 men, 32 women were compared on four measures before and after 3 weeks of rehabilitation. Measures were Beck Depression Inventory, Hamilton Anxiety Scale, Goldberg Scale, and Modified Borg Scale. In addition, a linear multiple regression model using age, gender, % predicted FEV(1), FEV(1)/FVC, % predicted DLCO as independent variables were used to predict changes. **RESULTS:** Patients who completed the pulmonary program showed significant changes in favour of post scores on all four scales at $p < 0.001$. The program significantly reduced anxiety and depression, and increased positive psychological outlook in severe pulmonary disease. Perceived breathlessness on the Borg Scale was significantly reduced ($p < 0.0001$). The multiple regression model was not statistically significant for prediction of any of the changes. **CONCLUSIONS:** Patients with severe pulmonary disease can significantly improve their psychological outlook and decrease anxiety and depression when they complete an inpatient pulmonary rehabilitation program. Psychological gains and perception of breathlessness improve with rehabilitation, even though FEV(1) and other pulmonary function tests may not predict these changes. A second implication is that rehabilitation improves psychological outlook with both severely ill patients and a group with mixed pulmonary and cardiac disease.

J Infect Dis. 2004 Jul 1;190(1):11-9. Epub 2004 May 26.

G

Immunity to influenza in older adults with chronic obstructive pulmonary disease.

Gorse GJ, O'Connor TZ, Newman FK, Mandava MD, Mendelman PM, Wittes J, Peduzzi PN.

Department of Veterans Affairs Medical Center and Division of Infectious Diseases and Immunology, Saint Louis University, St. Louis, Missouri, USA. gorsegj@slu.edu

BACKGROUND: Chronically ill older adults constitute a population vulnerable for complications associated with influenza. Study of their immunity to influenza virus may help design better strategies to stimulate protective immune responses. **METHODS:** Immunogenicity of influenza vaccines and immune protection from natural influenza were assessed in older adults with chronic obstructive pulmonary disease as part of a vaccine efficacy trial. Subjects received either trivalent inactivated influenza virus vaccine (TVV) intramuscularly and trivalent live cold-adapted influenza virus vaccine (CAIV-T; n=1107) intranasally (inl) or TVV and placebo inl (P; n=1108). **RESULTS:** In the subsets of study subjects assessed, serum hemagglutination inhibition (HAI) and nasal-wash antihemagglutinin (HA) immunoglobulin (Ig) A and IgG antibody levels and anti-influenza virus CD8(+) cytotoxic T lymphocyte activity increased after immunization. Mean postimmunization nasal-wash IgA antibody levels to influenza A H3/HA and B HA were statistically higher in the TVV+CAIV-T group (n=957) than in the TVV+P group (n=951). Postimmunization serum HAI and nasal-wash IgA antibodies to influenza A/H3N2 and B viruses were associated with a reduced relative risk for natural influenza infection. **CONCLUSIONS:** TVV+CAIV-T appeared more immunogenic than TVV+P, but the observed difference may be clinically unimportant. Anti-influenza serum and nasal-wash antibodies were associated with immune protection

Chest. 2004 Jun;125(6):2011-20.

I

Acute respiratory illness in patients with COPD and the effectiveness of influenza vaccination: a randomized controlled study.

Wongsurakiat P, Maranetra KN, Wasi C, Kositanont U, Dejsomritrutai W, Charoenratanakul S.

Division of Respiratory Disease and Tuberculosis, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand. sipwo@maidaol.ac.th

STUDY OBJECTIVES: To determine the effectiveness of influenza vaccination on influenza-related acute respiratory illness (ARI) and overall ARI in patients with COPD, and its relationship to the degree of airflow obstruction. **DESIGN:** Stratified, randomized, double-blind, placebo-controlled trial. **SETTING:** From June 1997 to November 1998 at a single university hospital. **Patients and interventions:** One hundred twenty-five patients with COPD were stratified based on their FEV(1) as having mild, moderate, and severe COPD. Within each group, they were randomized to the vaccine group (62 patients who received purified, trivalent, split-virus vaccine) or the placebo group (63 patients). **MEASUREMENTS:** The number of episodes and severity of total ARI, classified as outpatient treatment, hospitalization, and requirement of mechanical ventilation; and the number of episodes and severity of influenza-related ARI. **RESULTS:** The incidence of influenza-related ARI was 28.1 per 100 person-years and 6.8 per 100 person-years in the placebo group and vaccine

group, respectively (relative risk [RR], 0.24 [p = 0.005]; vaccine effectiveness, 76%). The incidences were 28.2, 23.8, and 31.2 per 100 person-years in the patients with mild, moderate, and severe COPD, respectively, in the placebo group, and 4.5, 13.2, and 4.6 per 100 person-years in the patients with mild, moderate, and severe COPD, respectively, in the vaccine group (RR, 0.16 [p = 0.06]; vaccine effectiveness, 84%; RR, 0.55 [p = 0.5]; vaccine effectiveness, 45%; and RR, 0.15 [p = 0.04]; vaccine effectiveness, 85%, in the patients with mild, moderate, and severe COPD, respectively). Bivariate analysis revealed that the effectiveness of influenza vaccination was not modified by the severity of COPD, comorbid diseases, age, gender, or current smoking status. There was no difference in the incidence or severity of total ARI between the placebo group and the vaccine group. CONCLUSIONS: Influenza vaccination is highly effective in the prevention of influenza-related ARI regardless of the severity of COPD. Influenza vaccination does not prevent other ARIs unrelated to influenza. The effectiveness of influenza vaccination in the prevention of overall ARI in patients with COPD will depend on how much the proportion of influenza-related ARI contributes to the incidence of total ARI. Influenza vaccination should be recommended to all patients with COPD.

Respirology. 2004 Jun;9(2):230-6.

G

Long-term effectiveness of an inpatient pulmonary rehabilitation program for elderly COPD patients: comparison between young-elderly and old-elderly groups.

Katsura H, Kanemaru A, Yamada K, Motegi T, Wakabayashi R, Kida K.

Pulmonary Division, and Rehabilitation Division, Tokyo Metropolitan Geriatric Medical Center, Tokyo, Japan. katsurah@saikuri.org

OBJECTIVE: To evaluate the long-term effects of pulmonary rehabilitation in elderly COPD patients, we monitored patients for 1 year after they completed a 2-week inpatient pulmonary rehabilitation program. We also compared the effects of pulmonary rehabilitation on young-elderly (age 65-74 years) and old-elderly (age 75 years or over) COPD patients. METHODOLOGY: Fifty-nine elderly COPD patients (mean age 72.8 years) were studied. They underwent a comprehensive 2-week inpatient pulmonary rehabilitation program incorporating 10 exercise sessions, each of which included endurance training of the lower extremities, peripheral muscle conditioning training of the upper and lower extremities, and stretching, along with various education sessions. The effects of pulmonary rehabilitation were evaluated at 3, 6, and 12 months after completion of the program. RESULTS: Overall, patient health-related quality of life (HRQoL) as assessed by a QoL scale, and dyspnoea as assessed by an oxygen cost diagram, improved significantly over the 12-month period. Exercise capacity assessed by a 6-min walking distance test (6MWD) was similarly significantly improved. However, there was some fall-off in terms of the distance walked 12 months after pulmonary rehabilitation. The improvements in exercise capacity, dyspnoea, and HRQoL did not differ between the two groups, with the exception that the 6MWD (P < 0.01) and the QoL scale (P < 0.05) at 3 months post-pulmonary rehabilitation were significantly higher in the old-elderly group. CONCLUSIONS: Pulmonary rehabilitation is an effective treatment in terms of improving dyspnoea, exercise capacity and HRQoL in elderly COPD patients, and the benefits are almost comparable for young-elderly and old-elderly patients.

Impact of preventing exacerbations on deterioration of health status in COPD.**Spencer S, Calverley PM, Burge PS, Jones PW.**Dept of Health and Social Care, Brunel University, Isleworth, UK.
Sally.Spencer@brunel.ac.uk

Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with worse health status. The Inhaled Steroids in Obstructive Lung Disease in Europe (ISOLDE) study showed that treatment with fluticasone propionate (FP) reduced exacerbation frequency and the rate of deterioration in health status as compared with placebo. The present study analysed these data to test whether the effect of FP on health status was attributable to its effect on exacerbations. Rates of deterioration in St George's Respiratory Questionnaire (SGRQ) total score were obtained for 613 patients with moderate to severe COPD followed for a maximum of 3 yrs. Exacerbation rates were skewed and could not be normalised, therefore, patients were stratified into three exacerbation groups: none, infrequent (<1.65 exacerbations x yr⁻¹) and frequent (>1.65 exacerbations x yr⁻¹). There were 91 patients with no exacerbations, 285 with infrequent exacerbations and 235 with frequent exacerbations. Frequent exacerbations were independently associated with a worse baseline SGRQ score ($p < 0.0001$) and a more rapid rate of deterioration in health status ($p = 0.0003$). Exacerbation frequency and rate of decline in forced expiratory volume in one second were independently related to the rate of deterioration in SGRQ score. Statistical modelling showed the beneficial effect of fluticasone propionate on deterioration in health status to be largely due to its effect on exacerbation frequency.

The last year of life of COPD: a qualitative study of symptoms and services.**Elkington H, White P, Addington-Hall J, Higgs R, Pettinari C.**Department of General Practice and Primary Care, Guy's King's and St. Thomas' School of Medicine, 5 Lambeth Walk, London SE11 6SP, UK.
helena.elkington@kcl.ac.uk

INTRODUCTION: To assess the symptoms experienced and their impact on patients' lives in the last year of life of COPD, and to assess patients' access to and contact with health services. **METHOD:** Qualitative analysis using the framework approach of in-depth interviews with 25 carers of COPD patients who had died in the preceding 3-10 months. **RESULTS:** The average age of death was 77.4 years. The majority of patients died in hospital. The major symptom reported by the carers was breathlessness which impaired the deceased's mobility and contributed to their being housebound. Anxiety and panic were also associated with breathlessness. Depression was reported. Oxygen, though beneficial, was seen to impose lifestyle restrictions due to increasing dependence on it. Some patients only health care contact was through repeat prescriptions from their GP whereas three had regular follow up by a respiratory nurse specialist who linked community and secondary care. Overall, follow-up, systematic

review or structured care were uncommon. DISCUSSION: Breathlessness causes major disability to patients with COPD in the last year of life. The expertise of palliative care in treating breathlessness may be valuable in these patients many of whom lacked regular health service contact in the year before death. Patients who are housebound with high levels of morbidity require community health services. Respiratory nurse specialists were rarely involved in the patients' care and may provide a link between the GP, the chest physician and the palliative care team.

Respiration. 2004 May-Jun;71(3):246-51.

G

Occupational therapy and pulmonary rehabilitation of disabled COPD patients.

Lorenzi CM, Cilione C, Rizzardi R, Furino V, Bellantone T, Lugli D, Clini E.

Division of Pneumology and Pulmonary Rehabilitation, Fondazione Villa Pineta ONLUS (Pavullo, MO) and University of Modena-Reggio Emilia, Italy.

BACKGROUND: Occupational therapy (OT) has been defined as a task of rehabilitation for disabled patients, giving them maximal function and independence to sustain specific activities of daily living. OBJECTIVES: To evaluate the effectiveness of OT as an adjunctive measuring during pulmonary rehabilitation (PR) of hospitalized COPD patients. METHODS: A prospective clinical trial with parallel groups was undertaken in severely disabled COPD patients (n = 71, age 73 +/- 5 years). They were assigned to either OT+PR (n = 47, FEV1 46 +/- 21%pred.) or PR (n = 24, FEV1 44 +/- 12%pred.). PR consisted of eighteen 3-hour daily sessions, whilst OT (domestic activities) was added 3 times a week up to nine 1-hour sessions. Six-min walk (6MWD) with evaluation of BORG dyspnea (D) and leg fatigue (F) scores at end of effort, breathlessness sensation (B) by means of the MRC scale as well as the number of functions lost in the Basic Activity of Daily Living (BADL) categories were assessed as outcomes before (T0) and after (T1) rehabilitation. RESULTS: 6MWD (from 165 +/- 63 to 233 +/- 66 and from 187 +/- 52 to 234 +/- 65 m in the OT+PR and PR groups, respectively), D (from 4.9 +/- 2.1 to 3.2 +/- 1.6 and from 5.3 +/- 2.1 to 3.4 +/- 2.1), F (from 6.1 +/- 0.5 to 4.5 +/- 1.7 and from 5.9 +/- 0.8 to 4.3 +/- 0.8) and B (from 4.3 +/- 0.9 to 3.0 +/- 0.9 and from 4.2 +/- 1.0 to 3.2 +/- 0.8) had similarly improved (p < 0.01) in both groups at T1. The percentage distribution of patients across the BADL categories significantly changed (p = 0.004) in OT+PR (from 17 to 61%, from 70 to 34% and from 23 to 5% in categories A, B and C, respectively) but not in the PR group. CONCLUSIONS: The addition of OT to comprehensive PR is able to specifically improve the outcome of severely disabled COPD inpatients. Copyright 2004 S. Karger AG, Basel

Aging Clin Exp Res. 2004 Feb;16(1):26-33.

G

Effects of chronic airway disease on health status of geriatric patients.

Antonelli Incalzi R, Pistelli R, Imperiale C, Catalano F, Scichilone N, Bellia V; Sa.R.A. Study Group.

Istituto di Medicina Interna e Geriatria, Catholic University, Roma, Italy.

BACKGROUND AND AIMS: The impact of chronic airway disease on the health status of elderly patients is only to some extent explained by indexes of airflow limitation. The present study was designed to assess to what extent: 1) asthma, chronic obstructive pulmonary disease (COPD) and chronic bronchitis with normal FEV1 (simple bronchitis) differ in their impact on health status; 2) health status depends upon non-respiratory factors. **METHODS:** A total of 1601 outpatients over 65-198 with asthma, 228 with COPD, 91 with simple bronchitis, and 1084 with non-respiratory illnesses (control group)--were studied by collection of five health status indexes and multidimensional assessment. Discriminant analysis was used to identify health status profiles of groups. Demographic, anthropometric, clinical and respiratory function correlates of selected health status profiles were identified. **RESULTS:** Only 26 and 28% of asthma and COPD patients vs 43% of simple bronchitis and 50% of non-respiratory patients showed group-specific health status profiles. These profiles were characterized by lower 6-min walked distance and greater index of disturbed sleep in asthmatics, and by worse performance on Barthel Index, 6-min walking test and Mini-Mental State Examination in COPD patients. More severe bronchial obstruction, a greater index of comorbidity and a longer occiput-wall distance characterized COPD patients with the worst health status. **CONCLUSIONS:** The health status of elderly patients with COPD or asthma is highly heterogeneous. On average, COPD is characterized by more severe physical impairment, and asthma by poorer quality of sleep. Comorbidity and severity of bronchial obstruction, but not age, contribute toward defining a subset of COPD patients with the worst health status.

Aging Clin Exp Res. 2004 Feb;16(1):13-21.

G

Management of chronic obstructive pulmonary disease in the elderly.

Antonelli

Incalzi

R.

Istituto di Medicina Interna e Geriatria (CEMI), Universita Cattolica, Roma, Italy.
raffaele_antonelli@rm.unicatt.it

Chronic obstructive pulmonary disease (COPD), a leading cause of death and disability in the elderly, is frequently unrecognized or misinterpreted as heart disease. Comorbidity plays a primary role, both as a determinant of health status and as a prognostic marker in older populations with COPD. Multidimensional assessment tailored to the distinctive needs of respiratory patients and thus including selected respiratory function indexes, is mandatory for proper staging COPD and monitoring of its course and response to therapy. In stable COPD, a mix of pharmacological and non-pharmacological measures may improve health, but only by stopping smoking and, in the event of respiratory insufficiency, applying continuous oxygen therapy can the progression of the disease be delayed and life expectancy prolonged. In exacerbated COPD, age per se is a negative prognostic marker and, while many very old patients can successfully recover, they will experience some decline in personal independence. Thus, older patients with COPD should ideally be the object of a continuum of care throughout all the stages of their disease, in order to minimize the decline in personal independence and worsening health. In this perspective, COPD patients qualify as optimal candidates for dedicated programs of continuous geriatric care.

Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study.

Miravittles M, Ferrer M, Pont A, Zalacain R, Alvarez-Sala JL, Masa F, Vereia H, Murio C, Ros F, Vidal R; IMPAC Study Group.

Servei de Pneumologia, Institut Clinic de Pneumologia i Cirurgia Toracica (IDIBAPS), Hospital Clinic, Barcelona, Spain. marcm@clinic.ub.es

BACKGROUND: A study was undertaken to evaluate exacerbations and their impact on the health related quality of life (HRQL) of patients with chronic obstructive pulmonary disease (COPD). **METHODS:** A 2 year follow up study was performed in 336 patients with COPD of mean (SD) age 66 (8.2) years and mean (SD) forced expiratory volume in 1 second (FEV(1)) 33 (8)% predicted. Spirometric tests, questions regarding exacerbations of COPD, and HRQL measurements (St George's Respiratory Questionnaire (SGRQ) and SF-12 Health Survey) were conducted at 6 month intervals. **RESULTS:** A total of 1015 exacerbations were recorded, and 103 (30.7%) patients required at least one hospital admission during the study. After adjustment for baseline characteristics and season of assessment, frequent exacerbations had a negative effect on HRQL in patients with moderate COPD (FEV(1) 35-50% predicted); the change in SGRQ total score of moderate patients with > or =3 exacerbations was almost two points per year greater (worse) than those with <3 exacerbations during the follow up (p = 0.042). For patients with severe COPD (FEV(1) <35% predicted) exacerbations had no effect on HRQL. The change in SGRQ total score of patients admitted to hospital was almost 2 points per year greater (worse) than patients not admitted, but this effect failed to show statistical significance in any severity group. There was a significant and independent seasonal effect on HRQL since SGRQ total scores were, on average, 3 points better in measurements performed in spring/summer than in those measured in the winter (p<0.001). **CONCLUSIONS:** Frequent exacerbations significantly impair HRQL of patients with moderate COPD. A significant and independent effect of seasonality was also observed.

Gaps in the care of patients admitted to hospital with an exacerbation of chronic obstructive pulmonary disease.

Choi PP, Day A, Etlchells E.

Department of Medicine, Sunnybrook and Women's College Health Sciences Centre and University of Toronto, Toronto, Ontario.

BACKGROUND: Patients admitted to hospital because of an exacerbation of chronic obstructive pulmonary disease (COPD) are at high risk of adverse events. We evaluated the association between gaps in care and adverse events during the hospital stay and after discharge. **METHODS:** We retrospectively reviewed the charts of 105 consecutive patients discharged from hospital between Jan. 1 and Dec. 31, 2001, with a diagnosis of COPD exacerbation. On the basis of published guidelines, prior studies and discussions with colleagues, we defined a care gap as having occurred if any of 9

important inpatient and 7 discharge-related processes of care did not take place correctly. Inpatient adverse events included worsening of condition after admission, transfer to a higher level of care, cardiac arrest and death. Discharge-related adverse events were defined as including readmission to the hospital, revisit to the emergency department or death within 30 days after discharge. RESULTS: Of the 105 patients studied, 88 (84%) had at least 1 inpatient gap in care and 16 (15%) an inpatient adverse event; 2 of the 16 died. Patients who had an inpatient adverse event had more gaps in their care (2.0 v. 1.3 gaps, $p = 0.004$) and longer stays (16.4 v. 8.6 days, $p = 0.007$). There were 6 adverse events (frequency 38%) among the 16 patients with 3 or more gaps in their care, 6 adverse events (28%) among the 21 patients with 2 gaps, 1 adverse event (2%) among the 51 patients with 1 gap and 3 adverse events (18%) among the 17 patients with no gaps in their care ($p = 0.001$ for trend). Of the 103 patients discharged alive, 102 (99%) had at least 1 gap in discharge-related care, but we found no association between these gaps and adverse events within 30 days after discharge. INTERPRETATION: Gaps in the inpatient care of patients with COPD exacerbation were common and were associated with inpatient adverse events. Gaps in discharge-related care were also common but were not associated with postdischarge adverse events.

Am J Phys Med Rehabil. 2004 May;83(5):337-43.

G

Minimally supervised home rehabilitation improves exercise capacity and health status in patients with COPD.

Ferrari M, Vangelista A, Vedovi E, Falso M, Segattini C, Brotto E, Brigo B, Lo Cascio V.

Dipartimento di Scienze Biomediche e Chirurgiche, Servizio di Fisiopatologia Respiratoria, Università di Verona, Verona, Italy.

OBJECTIVE: The purpose of this study was to investigate the effects on exercise tolerance and quality of life of an outpatient rehabilitation program implemented at home without a physiotherapist's direct supervision in patients with chronic obstructive lung disease. DESIGN: Patients with moderate chronic obstructive pulmonary disease were studied. The rehabilitation program included lower limb exercise on a stationary bicycle and upper limb exercise and stretching, together with education, and it lasted for 12 wks. Every 2 wks, a physiotherapist contacted patients by phone to evaluate their compliance with the rehabilitation program and any adverse effects. The main measures of outcome were the Health Status Index, cycle ergometer test, forced expiratory volume in 1 sec, and forced vital capacity. Patients were evaluated at the baseline and at 12 wks. RESULTS: A total of 32 patients were recruited and 28 (mean age, 70.4 yrs) completed the trial. After pulmonary rehabilitation, a significant improvement was found in seven of the nine Health Status Index quality-of-life subscales. Exercise tolerance also improved significantly, whereas no variation was observed in pulmonary function tests. There was no correlation between the improvement in quality of life and the improvement in exercise tolerance. The improvements in the Health Status Index physical function and general health subscales correlated negatively with forced expiratory volume in 1 sec (percentage of predicted value) and positively with residual volume/total lung capacity ratio. The improvement in exercise tolerance (expressed in watts or as maximum oxygen uptake), but not in quality-of-life indexes, was associated negatively with age and positively with weight, cognitive function, and forced expiratory volume in 1 sec/forced vital capacity ratio. CONCLUSIONS: We conclude that an inexpensive home

rehabilitation program can improve quality of life and exercise tolerance in patients with moderate chronic obstructive pulmonary disease. Furthermore, our results indicate that exercise tolerance evaluated by cycloergometry and quality of life evaluated by the mean of the Health Status Index questionnaire are independent outcome measures of pulmonary rehabilitation.

Respir Med. 2004 Apr;98(4):351-6.

I

Cognitive performance in patients with COPD.

Liesker JJ, Postma DS, Beukema RJ, ten Hacken NH, van der Molen T, Riemersma RA, van Zomeren EH, Kerstjens HA.

Department of Pulmonary Diseases, University Hospital Groningen, Hanzeplein 1, Postbox 30001 NL-9700-RB, Groningen, The Netherlands.

BACKGROUND: Hypoxemic patients with Chronic Obstructive Pulmonary Disease (COPD) have impaired cognitive performance. These neuropsychological impairments are related to the degree of hypoxemia. So far, cognitive performance has not been tested in non-hypoxemic patients with COPD. **METHODS:** We recruited patients with stable COPD and PaO₂ > 8.0 kPa (60 mmHg), as well as healthy subjects, who were matched for age, intelligence quotient (IQ), and level of education. Cognitive performance was studied by Stroop Colour Word Test, Trailmaking, digit-symbol of the Wechsler Adult Intelligence Scale, addition subtest of the Groningen Intelligence Test, and Story Recall. **RESULTS:** Thirty patients with COPD (FEV₁ 49.8% pred, mean age 64.8 yr) and 20 healthy volunteers (65.6 yr) were enrolled. COPD patients performed significantly worse on trailmaking B, the digit-symbol test, and on the addition subtest. There was no significant correlation between the tests of cognitive performance and disease specific health status (Chronic Respiratory Questionnaire). **CONCLUSIONS:** We conclude that even non-hypoxemic patients with COPD show significant impairments in cognitive performance. These impairments are not associated with deteriorations in health related quality of life. Prospective evaluation of the impact of treatment on cognitive performance in non-hypoxemic patients with COPD would be a logical subsequent study.

J Sleep Res. 2004 Mar;13(1):79-86.

Does cognitive dysfunction conform to a distinctive pattern in obstructive sleep apnea syndrome?

Antonelli Incalzi R, Marra C, Salvigni BL, Petrone A, Gemma A, Selvaggio D, Mormile F.

Department of Gerontology, Università Cattolica del Sacro Cuore Geriatric Outpatient Department ASL RM E, Rome, Italy.

Obstructive sleep apnea (OSA) is a recognized cause of cognitive dysfunction. By using a cross-sectional comparative study, we aimed to verify whether neuropsychological performance of untreated OSA patients conforms to a distinctive pattern. Forty-nine newly diagnosed, untreated OSA patients, 27 with multi-infarctual dementia (MID), 31 with mild to moderate dementia of Alzheimer type (DAT) and 63 with severe chronic obstructive pulmonary disease (COPD), all free from major

comorbid dementing conditions were chosen for the study. The groups were matched for age and education. We found a bimodal distribution of cognitive performance in OSA group, which was therefore divided into two clusters having better (OSAb, n = 35) and worse (OSAw, n = 14) performance on a battery of 10 cognitive indexes. Cognitive performances of OSAb, OSAw, MID, DAT and COPD were compared by discriminant analysis. OSAb performed better than OSAw in all but one test. Deductive thinking and verbal attainment were more severely impaired in OSAw than in COPD patients. Constructive ability, deductive thinking and both verbal attainment and immediate memory were comparably impaired in OSAw and DAT. The mean neuropsychological scores of OSAw and MID were comparable, but 71% of OSAw patients had a distinctive cognitive profile, i.e. a group specific pattern of cognitive dysfunction, according to discriminant analysis. One of four newly diagnosed OSA patients had a severe and distinctive neuropsychological dysfunction mainly involving inductive and deductive thinking, and constructive ability. Some analogy with cognitive pattern of MID suggests that a mainly subcortical damage underlies this dysfunction.

Am J Respir Crit Care Med. 2004 Jun 15;169(12):1298-303. Epub 2004 Feb 27.

I

Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease.

Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA.

Academic Unit of Respiratory Medicine, St Bartholomew's Hospital, London, UK.

Treatment of chronic obstructive pulmonary disease (COPD) exacerbations improves outcomes; however, responses to treatment are variable, and patients with COPD often delay presentation or fail to seek therapy. The impact on exacerbation outcomes, hospitalization, and health status of delaying or failing to seek treatment is poorly understood. We studied between 1996 and 2002 a cohort of 128 patients with COPD, mean (SD) FEV(1) of 1.07 (0.43) L. Patients recorded respiratory symptoms daily and reported exacerbations to the outpatient-based study team or to their primary care physician; 1,099 exacerbations were recorded by the patients, of which 658 were reported to a physician. The time between exacerbation onset and treatment was a median (interquartile range) of 3.69 (2.0-5.57) days, and the exacerbation recovery time was 10.7 (7.0-14.0) days. Earlier treatment was associated with a faster recovery (regression coefficient 0.42 days/day delay) (confidence interval, 0.19-0.65; $p < 0.001$). Patients who reported a higher proportion of exacerbations for treatment had better health-related quality of life than those patients with more untreated exacerbations ($\rho = -0.22$, $p = 0.018$). Failure to report exacerbations was associated with an increased risk of emergency hospitalization ($\rho = 0.21$, $p = 0.04$). Patient recognition of exacerbation symptoms and prompt treatment improves exacerbation recovery, reduces risks of hospitalization, and is associated with a better health-related quality of life.

Thorax. 2004 Mar;59(3):204-9.

G

Association between air pollution exposure and exhaled nitric oxide in an elderly population.

Adamkiewicz G, Ebelt S, Syring M, Slater J, Speizer FE, Schwartz J, Suh H, Gold DR.

Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA. gadamkie@hsph.harvard.edu

BACKGROUND: Animal models suggest that the cardiovascular effects of air pollution result in part from inflammation caused by proinflammatory mediators originating in the lung. In a human study of the cardiovascular effects of air pollution, we aimed to evaluate the potential association between air pollution levels and the fraction of exhaled nitric oxide (FE(NO)), a non-invasive measure of airway inflammation. **METHODS:** Breath samples were collected weekly between September and December 2000 in a community based group of elderly subjects (median age 70.7 years) in Steubenville, Ohio. The samples were analysed for NO. Air pollution levels were measured concurrently at a central site monitor. **RESULTS:** An increase in the 24 hour average PM(2.5) concentration of 17.7 micro g/m(3) was associated with an increase in FE(NO) of 1.45 ppb (95% CI 0.33 to 2.57) in models adjusted for subject, week of study, day of the week, hour of the day, ambient barometric pressure, temperature, and relative humidity. This represents a change of approximately 15% compared with the mean FE(NO) in the cohort (9.9 ppb). A significant association was also observed for a 24 hour moving average of ambient NO (0.83 ppb increase, 95% CI 0.26 to 1.40). In two-pollutant models, the magnitude and precision of the PM(2.5) effect was not reduced and the ambient NO effect was no longer significant. The associations between FE(NO) and PM(2.5) were significantly higher in subjects with a doctor's diagnosis of COPD (p value for interaction = 0.03). **CONCLUSIONS:** Ambient pollution may lead to airway inflammation as measured by FE(NO). These subclinical inflammatory changes may be an important step in the pathogenesis of the cardiopulmonary effects induced by exposure to air pollution.

Chest. 2004 Feb;125(2):473-81.

I

Prospective multicenter study of relapse following emergency department treatment of COPD exacerbation.

Kim S, Emerman CL, Cydulka RK, Rowe BH, Clark S, Camargo CA; MARC Investigators.

Department of Emergency Medicine, Massachusetts General Hospital, 55 Fruit Street, Clinics Building 397, Boston, MA 02114, USA.

STUDY OBJECTIVES: To determine the incidence and risk factors of relapse after an emergency department (ED) visit for COPD exacerbation. **DESIGN:** Prospective cohort study as part of the Multicenter Airway Research Collaboration. **SETTING:** Twenty-nine North American EDs. **PATIENTS:** ED patients with COPD exacerbations, age > or =55 years. For the present analysis of post-ED relapse, the cohort was restricted to COPD patients who had been discharged from the ED directly to home. **Measurements and results:** Eligible patients underwent a structured interview to assess their demographic characteristics, COPD history, and details of the current COPD exacerbation. Data on ED medical management and disposition were obtained by chart review. Patients were contacted by telephone 2 weeks later regarding incident relapse events (ie, urgent clinic or ED visit for worsening COPD). The cohort consisted of 140 COPD patients. Over the next 2 weeks, patients demonstrated a consistent daily relapse rate that summed to 21% (95% confidence interval, 15 to 28%) at day 14. In a multivariate

model, the significant risk factors for relapse were the number of urgent clinic or ED visits for COPD exacerbation in the past year (odds ratio [OR], 1.49 [per five visits]), self-reported activity limitation during the past 24 h (OR, 2.93 [per unit on scale of 1 [none] to 4 [severe]]), and respiratory rate at ED presentation (OR, 1.76 [per 5 breaths/min]). CONCLUSIONS: Among patients discharged to home after ED treatment of a COPD exacerbation, one in five patients will experience an urgent/emergent relapse event during the next 2 weeks. Both chronic factors (ie, a history of urgent clinic or ED visits) and acute factors (ie, activity limitations and initial respiratory rate) are associated with increased risk. Further research should focus on ways to decrease the relapse rate among these high-risk patients. The clinicians may wish to consider these historical factors when making ED decisions.

Crit Care Med. 2004 Feb;32(2):372-7.

G

Noninvasive ventilation in patients with acute hypercapnic exacerbation of chronic obstructive pulmonary disease who refused endotracheal intubation.

Chu CM, Chan VL, Wong IW, Leung WS, Lin AW, Cheung KF.

Department of Medicine and Geriatrics, United Christian Hospital, Kowloon, Hong Kong, SAR, China.

OBJECTIVE: To determine the long-term outcome of noninvasive ventilation in chronic obstructive pulmonary disease patients who refused intubation for acute hypercapnic respiratory failure. DESIGN: Prospective, observational study. SETTING: Noninvasive ventilation unit in an acute regional hospital in Hong Kong. METHODS: The study recruited 37 chronic obstructive pulmonary disease patients who had the do-not-intubate code and developed acute hypercapnic respiratory failure. They were offered noninvasive ventilation, and their long-term outcomes were followed. Survival and event-free survival (an event is death or recurrent acute hypercapnic respiratory failure) were analyzed by survival analysis. Their disease profile and outcome were compared with another 43 chronic obstructive pulmonary disease patients without the do-not-intubate codes, who had acute hypercapnic respiratory failure and received noninvasive ventilation during the study period (usual care group). RESULTS: Patients in the do-not-intubate group were significantly older ($p = .029$), had worse dyspnea score ($p < .001$), worse Katz Activities of Daily Living score ($p < .001$), worse comorbidity score ($p = .024$), worse Acute Physiology and Chronic Health Evaluation II score ($p = .032$), lower hemoglobin ($p = .001$), and longer stay in the hospital during the past year ($p = .001$) than patients who received usual care. In the do-not-intubate group, the median survival was 179 days, and 1-yr actuarial survival was 29.7%; in the usual care group, the median survival was not reached during follow-up, and 1-yr actuarial survival was 65.1% ($p < .0001$). In the do-not-intubate group, the median event-free survival was 102 days, and 1-yr event-free survival was 16.2%; in the usual care group, median event-free survival was 292 days, and 1-yr event-free survival was 46.5% ($p = .0004$). CONCLUSIONS: A 1-yr survival of about 30% was recorded in chronic obstructive pulmonary disease patients with the do-not-intubate code who developed acute hypercapnic respiratory failure requiring noninvasive ventilation. The majority of survivors developed another life-threatening event in the following year. Information generated from this study is important to physicians and chronic

Am J Respir Crit Care Med. 2004 Apr 1;169(7):855-9. Epub 2004 Jan 07.

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Fracture risk associated with inhaled corticosteroid use in chronic obstructive pulmonary disease.

Lee TA, Weiss KB.

Midwest Center for Health Services and Policy Research, Hines VA Hospital, Hines, IL 60141, USA. lee@research.hines.med.va.gov

Patients with chronic obstructive pulmonary disease (COPD) are frequently treated with inhaled corticosteroids (ICS). However, the impact of ICS use on fracture risk remains unclear in these patients. This nested case-control study examines the association between ICS use and nonvertebral fractures in Veterans Affairs patients with COPD. From a cohort of 40,157 patients with a COPD diagnosis between October 1, 1998 and September 30, 1999, and that used services in the preceding 12-month period but did not have a COPD diagnosis, 1,708 cases with nonvertebral fractures were identified and matched to 6,817 control patients. Patients were 94% male, and average age was 62.7 years. ICS exposure was identified through prescription records and converted to beclomethasone equivalents. In conditional logistic regression models, exposure to ICS at any time during follow-up was not associated with an increased fracture risk (adjusted odds ratio = 0.97; 95% confidence interval, 0.84-1.11). However, current high-dose ICS users (> or = 700 microg per day) had an increased risk of fractures compared with patients with no exposure (adjusted odds ratio = 1.68; 95% confidence interval, 1.10-2.57). In patients with COPD, current use of high-dose ICS was associated with an increased risk of nonvertebral fractures.

American Journal of Respiratory and Critical Care Medicine Vol 170. pp. 1302-1309, (2004)
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Loss of Bone Density with Inhaled Triamcinolone in Lung Health Study II

Paul D. Scanlon, John E. Connett, Robert A. Wise, Donald P. Tashkin, Thelma Madhok, Melissa Skeans, Paul C. Carpenter, William C. Bailey, A. Sonia Buist, Michael Eichenhorn, Richard E. Kanner and Gail Weinmann the Lung Health Study Research Group

N. B. age=40-69, mean 57

Inhaled glucocorticosteroids (ICS) are commonly prescribed for chronic obstructive pulmonary disease. No adverse effect on bone mineral density (BMD) has been proven. In a randomized double-blind, placebo-controlled trial at seven centers in North America, we recruited 412 current smokers or recent quitters with mild to moderate chronic obstructive pulmonary disease. They used inhaled triamcinolone acetonide, 600 mcg, or placebo, twice daily. We measured femoral neck and lumbar spine BMD at baseline and after 1 and 3 years, and serum osteocalcin at baseline, 3 months, 1 year, and 3 years. After 3 years, BMD at the femoral neck decreased 1.78% more with ICS than with placebo ($p < 0.001$). More participants in the ICS group experienced 6% or more loss of femoral neck BMD ($p = 0.002$). Lumbar spine BMD increased in the placebo group by 0.98% but decreased by 0.35% in the ICS group (a difference of 1.33%, $p = 0.007$). Changes in osteocalcin did not correlate with changes in BMD. Fractures, lost height, or osteoporosis diagnoses were not increased among ICS users compared with placebo users. In summary, the use of inhaled triamcinolone

acetonide was associated with loss of BMD at the femoral neck and lumbar spine after 3 years of treatment.

Key Words: bone density • obstructive lung diseases • osteoporosis • randomized controlled trials • triamcinolone acetonide

American Journal of Respiratory and Critical Care Medicine Vol 170. pp. 1286-1293, (2004)
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Associated Loss of Fat-free Mass and Bone Mineral Density in Chronic Obstructive Pulmonary Disease

Charlotte E. Bolton, Alina A. Ionescu, Kathleen M. Shiels, Rebecca J. Pettit, Peter H. Edwards, Michael D. Stone, Lisette S. Nixon, William D. Evans, Timothy L. Griffiths and Dennis J. Shale

We hypothesized that in patients with chronic obstructive pulmonary disease, loss of fat-free mass (FFM) and loss of bone mineral density (BMD) were related to (1) each other and may be clinically inapparent, (2) urinary markers of cellular and bone collagen protein breakdown, and (3) severity of lung disease. Eighty-one patients and 38 healthy subjects underwent dual-energy X-ray absorptiometry to determine body composition and BMD. Urinary protein breakdown markers, inflammatory mediators, and their soluble receptors were determined. Thirty-three patients had a low fat-free mass index (kg/m^2), 17 of whom had a normal body mass index. Thirty-two percent of patients (13% of healthy subjects) had osteoporosis at the hip or lumbar spine. The marker of cellular protein breakdown was elevated in patients and related to lung disease severity and body composition. The marker of bone collagen breakdown was greater in patients with osteoporosis. Inflammatory mediators were elevated in patients. Loss of FFM and loss of BMD were related, occurred commonly, and could be subclinical in patients with chronic obstructive pulmonary disease. Loss of both was greatest with severe lung disease. Increased excretion of cellular and bone collagen protein breakdown products in those with low FFM and BMD indicates a protein catabolic state in these patients.

Key Words: body composition • dual-energy X-ray absorptiometry • osteoporosis