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Ventilatory restrictive impairment in thalassemic patients: Gender differences and correlation with hypogonadism and iron overload

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Background and aim: Ventilatory restrictive (RES) impairment has been described in β-thalassemia, but no evidence exists on the causal mechanism. We investigated relationships among lung function, iron overload and clinical parameters in a homogeneous series of β-thalassemia major adult patients.
Methods: We studied 79 patients (males M/females F 44/35; age 34.5±6.8 years) with β-thalassemia major on regular transfusion and iron chelation. Iron overload was assessed by serum ferritin, liver iron concentration (LIC) by SQUID susceptometry, cardiac iron by MRI T2*. Lung volumes, diffusion capacity, chelator drugs, hypogonadism (H), hypothyroidism and osteoporosis were evaluated in stable hematologic conditions.
Results: 30/79 pt (38%) [21/44 (47.7%) M and 9/35 (25.7%) F] showed RES, 6 bronchial obstruction with no gender differences (3M 3F). In F LIC was higher 2249±903 vs 1497±553 mgFe/gliver dw; p<0.008 in RES vs normals and correlated with total lung capacity (r=-0.402 p<0.03). No differences were present for hypothyroidism, osteoporosis or 3 iron chelators. Among RES patients 57%M and 88%F were H. H males showed higher cardiac iron MRI T2* 29.6±12.7 vs 39.6±9.2 ms; p<0.03) but similar LIC in respect to non H, without correlation with total lung capacity. In F cardiac and hepatic iron levels were not different between H and non H.
Conclusions: RES is present in 1/3 of well compensated adult thalassemic (M/F 1.88). Iron (LIC) was higher in RES F vs normals and H males have higher MRI T2*. Different gender impact of H on lung and chest growth, severity and efficacy of replacement therapy can explain data but the involved mechanisms is still unclear.

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Coexistent granulomatosis with polyangiitis (Wegener's) and Crohn disease: A clinicopathologic description of cases

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Background: Crohn disease (CD) may lead to various extraintestinal manifestations, including, rarely, respiratory tract involvement. When necrobiotic pulmonary nodules are present, the differential diagnosis includes granulomatosis with polyangiitis (Wegener's) (GPA). The respiratory tract manifestations of CD and GPA may mimic each other, complicating the diagnosis and suggesting the possible coexistence of these two conditions.
Aims: To describe the clinical, radiographic and histopathologic features of patients in whom CD and GPA coexist.
Methods: We reviewed the teaching files of the authors and searched the Mayo Clinic medical records for coexistent inflammatory bowel diseases and ANCA-associated vasculitides of the lungs. We reviewed in detail 97 patient charts, and excluded cases of ulcerative colitis and those in whom only one of the diagnoses was present or pathology slides were unavailable. Pulmonary and gastrointestinal biopsies were reviewed for the cases included in the study.
Results: Four cases were identified (2 women and 2 men, age range: 25-62). The diagnosis of CD preceded that of GPA in all cases. PR3/c-ANCA was positive in two cases, while in the other two PR3- and MPO-ANCA were both negative. Chest imaging showed pulmonary nodules in all cases. Pathology revealed features diagnostic of GPA in all cases with necrotizing granulomatous inflammation and segmental vasculitis. In addition, one case showed capillaritis.
Conclusion: Pulmonary findings in patients with CD, or the presence of granulomatous colitis in patients with GPA should prompt the inclusion in the differential diagnosis of a possible coexistence of CD and GPA.

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Arterial hypoxaemia in morbid obesity

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Introduction: Morbid obesity (MO) can be associated with arterial hypoxaemia, mostly due to a highly prevalent obstructive sleep apnoea (OSA).
Objective: To determine the prevalence of hypoxaemia in patients with MO before and one year after bariatric surgery (BS) and its correlation with OSA.
Methods: We included 230 patients (44± [SD] 12 yrs; 165 females; BMI, 46±7 kg/m^2; and, waist-to-hip-ratio, 0.96±0.08). OSA was defined as an apnoea/hypopnoea index (AHI) ≥10.
Results: Before BS, all patients (ERV, 33±22%) had spirometry and DLCO within reference values, with normal PaO2 (83±12 mmHg) and PaCO2 (36±3 mmHg) values. One hundred and fifty four (70%) patients had OSA (48%, severe OSA [AHI ≥30]), 66 (43%) with hypoxaemia (PaO2, 70±7 mmHg). Patients with OSA had lower PaO2 and higher PaCO2 than those without OSA (p <0.05 each). Thirty out of 230 patients (13%) without OSA had hypoxaemia (PaO2, 74±4 mmHg), whose FVC, FEV1, VC, IC, ERV and DLCO were lower than those in 36 normoxaemic (PaO2, 93±7 mmHg) patients (p<0.01 each). Overall PaO2 was correlated with waist-to-hip-ratio (r, −0.30, p<0.05). Before BS, age, sex, FVC, ERV and waist-to-hip-ratio were the independent factors associated with hypoxaemia (r2, 0.28, p<0.05) (multiple regression analysis). After BS, patients had a 76±18% of excess weight loss with overall improvement in lung function (p<0.01 each) while OSA ameliorated in 65% of them. Post-BS ERV (115±37%) and PaO2 (93±10 mmHg) improvements (p<0.01 each) were associated (r, 0.22, p<0.05).
Conclusions: Hypoxaemia continues to be a common finding in MO, mostly in patients with OSA. However, hypoxaemia can also be present without OSA, possibly related to central obesity.
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Hypoxic challenge assessments in patients with obesity hypoventilation syndrome

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Background: With worldwide increase in obesity and air travel, more obese people are likely to travel by air in future. No prospective studies have investigated the degree of arterial hypoxaemia during a hypoxic challenge test (HCT) in patients with obesity hypoventilation syndrome (OHS).
Objectives: To investigate the likelihood of a positive HCT in patients with OHS

who are not hypoxaemic at sea level and any possible predictors of desaturation during HCT.
Methods: Ten patients with OHS treated with long term nocturnal non invasive ventilation (NIV) were recruited. Clinically unstable patients and those with COPD were excluded. HCT was part of a detailed assessment and consisted of breathing 15% oxygen via a Douglas bag for 20 minutes.
Results: Mean age 57.4 years (±12.4) and mean BMI 52.8 (±13.3). Seven out of ten had a positive HCT (PaO2 < 6.6 kPa or SpO2 < 85%). Arterial blood gas was attempted in all but could not be taken in two patients. Mean PaO2 before and during HCT was 10 kPa (±0.4) and 6.2 kPa (±0.5) respectively. Mean PaCO2 before and during HCT was 5.5 kPa (± 0.8) and 5.3 kPa (±0.8) respectively. Baseline PaCO2 correlated negatively with PaO2 and SpO2 during HCT (r= -0.823, p=0.012 and r= -0.795, p=0.018 respectively). BMI, baseline PaO2 and SpO2, distance walked and minimum SpO2 during ISWT were not significantly correlated with the PaO2 or SpO2 during HCT.
Conclusion: Seventy percent of these patients had a positive HCT despite adequate control of their ventilatory failure. Baseline PaCO2 but not the PaO2 or SpO2 was predictive of a positive HCT. Although these results need to be confirmed in larger studies, we suggest assessment of these patients including a HCT before air travel.

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Pulmonary involvement in patients with Marfan syndrome
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Pulmonary involvement is not generally considered a main feature of Marfan syndrome, an autosomal connective tissue disorder caused by mutations in the extracellular matrix protein fibrillin1 particularly affecting vascular, skeletal and ocular systems. However, thanks to the substantial progress in treatments, life expectation of these patients has been dramatically improved in the last 20 years determining changes in different organ systems. The number of patients with a degree of underlying pulmonary pathology may be higher than expected. Clinical history, chest CT, spirometry, lung volumes,and diffusing capacity have been assessed in 64 patients of our national referral center (mean age 32±14 years; M 45%). None of the patients reported chronic respiratory symptoms and only 5 were smokers. Fourteen per cent reported a previous pneumothorax and 2 of them underwent surgery. Three reported bullae and 1 underwent bullectomy. Eleven per cent had radiological signs of emphysema and 32% apical blebs.Twenty-three per cent had cardiothoracic surgery. Forty-five per cent had moderate to severe rib cage abnormalities; 4 of them underwent repeated surgical corrections. Only 37% of our patients had normal lung function; 19% showed a restrictive pattern and 44% an obstructive pattern or an isolated diffusion impairment or an isolated hyperinflation. All patients with previous pneumothorax showed an obstructive pattern and diffusion impairment. In conclusion, in the absence of respiratory symptoms, pulmonary abnormalities should be actively detected and monitored and particular attention should be paid to prevent pneumothorax. Our results support the importance of lung volume determination and, when needed, chest CT in Marfan patients.

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Lung function abnormalities in patients with heart failure and preserved ejection fraction
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Introduction: Heart failure with preserved ejection fraction (HFPEF) accounts for 40-50% heart failure patients. The aim of this study was to evaluate the prevalence, type and severity of lung function abnormalities among outpatients with HFPEF.
Methods: In this prospective, descriptive study we included consecutive outpatients with new onset of HFPEF according with the European Society of Cardiology criteria. All underwent a clinical evaluation, chest X-ray, electrocardiogram, echocardiography, brain natriuretic peptide determination, forced spirometry, lung volumes by body plethysmography, single-breath carbon monoxide diffusing capacity (DLCO) corrected for alveolar volume and arterial blood gases.
Results: We included 63 outpatients (68% females), mean age 77 years. Mean body mass index 29.8 kg/m^2. 85% had arterial hypertension. 25.4% former smokers and 4.8% active smokers. 71.4% did not report any known respiratory diagnosis. Complete lung function evaluation was available in 50 patients, 88% showed abnormal results: 30% had evidence of airflow limitation (mild 7%, moderate 53%, severe 40%), 16% restrictive ventilatory defect (mild 75%, moderate 25%), mixed pattern 14%. DLCO was abnormal in 82%(mild 63.4%, moderate 29.2%, severe 7.3%). Correction by alveolar volume was complete in 39%, partial 46% and 14,6% did not correct. Arterial blood gases were measured in 45 patients, 67% had hypoxemia (mild 63.3%, moderate 26.6%, severe 10%).
Conclusions: Patients with HFPEF show a high prevalence of lung function abnormalities. Most are underdiagnosed and may contribute to their symptoms. Their pathophysiology is likely multifactorial (smoking, obesity, age, heart function) but requires further research.

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Patients with tissue hypoxia with unknown origin
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Background: Dyspnoea is common complication in respiratory disease and is mainly caused by hypoxemia due to lung diseases, cardiac diseases or neurologic diseases. Patients with dyspnoea without hypoxemia, hypercapnia and clear abnormal findings considered to have psychological problems. We have found a group of some patients who complain dyspnoea without hypoxemia (normal SpO_2 and PaO_2) have high venous oxygen level (P_vO_2). The aim of this study was to investigate the clinical characteristics of patients who have high PvO_2 and normal SpO_2.
Method: Eight patients have dyspnoea with high PvO_2 with normal SpO_2 were enrolled in this study. Patients with any other lung diseases or systemic diseases, abnormal chest X-ray finding or elevation of inflammatory markers were also excluded. Arterial and venous blood gas analysis was performed after 10 minutes bed rest. Tissue oxygen levels (PtO_2) was calculated using following equation; $PtO_2=PaO_2-PvO_2$. Serum lactate and pyruvate level were measured by enzyme assay.
Results: PvO_2 in patients enrolled (67.3±12.4 mmHg) was higher than normal range (26-40 mmHg) and PtO_2 in patients enrolled was lower (22.0±17.3 mmHg,normal range: 40-70 mmHg) than normal range. Serum lactate(21.6±7.9 mg/dl) and pyruvate(2.1±0.9 mg/dl) were also elevated compared to normal range.
Discussion and conclusion: The group of patients seem to have dyspnoea due to tissue hypoxia. The tissue hypoxia probably raises pyruvate and lactate levels due to activation of anabolic glycolysis. PvO_2 measurement and assessment of tissue hypoxia is need for the patients with dyspnoea without hypoxemia. It would be also necessary to explore the cause of tissue hypoxia in the patients.

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Lung cancer as a comorbidity in idiopathic pulmonary fibrosis (IPF)
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Introduction: IPF is associated with an increased risk for lung cancer. This might be explained by a contribution of IPF to lung cancer (LC) development or a role of LC in IPF development and/or by shared pathomechanisms causing both IPF and LC. However, data on incidence and reports on treatment related complications are limited.
Methods: In a retrospective monocenter analysis, patients (pts) who were diagnosed between 1/2004-12/2011 with IPF according to the current ATS/ERS guideline were reviewed for the diagnosis of LC.
Results: Of 229 IPF pts, 28 had IPF with LC (12%): 92% male, median age 67 years, median 39.5 pack years, median VC 82% pred., TLC 81% pred, TLCO-SB 35% pred. 75% had NSCLC with stages IA (5%), IB (10%), IIIA (29%), IIIB (10%), IV (29%), not further specified (17%). 25% had SCLC with 43% limited and 57% extensive disease. Diagnosis was simultaneous in 41%, IPF diagnosis prior to LC in 44% (median delay 36 months) and after LC diagnosis in 15% (median delay 5 months). 7 pts received surgery, 4 chemotherapy, 4 chemo-radiotherapy, 7 radiotherapy and 6 best supportive care for treatment of LC. Complications were common with myocardial infarction in 3 pts after surgery and 1 during chemo-radiotherapy, pneumonia in 6 pts (4 after surgery, 2 during chemotherapy) and radiation pneumonitis in 4 pts. 30 days mortality after surgery was 29%.
Conclusions: LC is a frequent comorbidity in IPF where an interdisciplinary evaluation of therapeutic options is mandatory. However, treatment related complications, especially after surgery are high. Prognosis of operable patients with IPF and LC might be decreased compared to patients either suffering from IPF or with LC alone.