208. Novelties in clinical management of thoracic diseases: from diaphragm to pleura

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The role of nerve transplantation in the management of symptomatic diaphragm paralysis

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Diaphragm paralysis may cause symptomatic respiratory disturbances, and often occurs as a result of iatrogenic or traumatic phrenic nerve injury. Treatment options have been limited to plication of the diaphragm, however it is likely that most patients receive no therapeutic intervention regardless of the severity of symptoms. Although nerve transplantation is efficacious for various peripheral nerve injuries, it has only begun to be established for analogous conditions involving the phrenic nerve.

Thirty consecutive patients presenting with chronic, symptomatic phrenic nerve injuries following surgery, chiropractic manipulation, trauma or anesthetic blocks underwent a comprehensive evaluation, including radiographic and electrophysiologic assessments. Inclusion criteria consisted of patients who failed to improve

during six months of conservative management, in whom a clear etiology for phrenic nerve injury could be elicited and confirmed with pre-operative evaluation. Measures of post-operative improvement included: pulmonary function testing, chest fluoroscopy, and a standardized quality-of-life survey.
Reversal of diaphragm paralysis was clearly demonstrated in 77% of patients (23/30) following nerve transplantation. In four patients (13%) there was no clinical or radiographic evidence of diaphragm function after 18 months, whereas in the remaining three patients (10%) it was too early to determine if surgical intervention was successful. There were no pulmonary or cardiac complications.
Nerve transplantation may reverse phrenic nerve injury and should be considered as an effective treatment option in the management of symptomatic diaphragm paralysis.

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Failure of Nissen fundoplication in chronic cough: Evidence for gaseous reflux

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Introduction: Accurate diagnosis and management of airway reflux induced chronic cough is challenging. Nissen Fundoplication (NF) is a recognised treatment option for patients who fail medical treatment. Unfortunately some patients continue to be symptomatic even after NF.
Aim: To assess pharyngeal gaseous pH in patients who failed to respond to NF
Methods: Retrospective case review of 22 patients who remained symptomatic post NF at Castle Hill Hospital, UK. All subjects had pre-NF oesophageal manometery, 24 hours ambulatory PH monitoring and a post -NF airway pH measurement using Restech Dx-pH measurement system. Some of these patients had follow up 24 hour ambulatory PH monitoring.
Results: Total of 22 patients (18 female) with a mean age of 45(range22-72) constituted the study population. All of these patients continued to have troublesome cough evidenced by a high Hull Cough Hypersensitivity Score with a mean score of 39(range 25-66), normal < 12.
15(68%) of these patients had an abnormal airway pH study with a mean upright Ryan score of 145(range17.72-573.46), normal < 9.41. All of the 7 patients who had 24 hour oesophageal pH monitoring had a normal DeMeester score with a mean of 3.47(range0.5-11.7), normal < 14.72.Out of the 7 with normal DeMeester 5 had an abnormal airway PH with a mean Ryan score of 175.28(range17.5-573.46).
Conclusion: The data suggest that NF eliminated significant acid liquid reflux. A significant proportion of patients continued to have airway gaseous reflux as evidenced by a positive Ryan score. This implies that the aetiology of chronic cough lies in impaction of gaseous reflux in the pharynx and upper airways rather than the liquid reflux detected on conventional testing.

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Proadrenomedullin improves the prognostic property of the BODE index

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Background: The BODE index, a multidimensional grading system assessing the respiratory and systemic expressions of COPD, proved helpful in the prognostic assessment in COPD. We hypothesize that systemic biomarkers might additionally improve categorization and outcome prediction in COPD.
Methods: We prospectively evaluated 638 patients with stable COPD for ≥ 6 weeks, > 10 PY and GOLD II-IV seeking care in pulmonary tertiary hospitals in 8 European countries and included in the PROMISE cohort. The primary outcome of the study was death from any cause and from respiratory causes. Median observation time was 24 months.
Results: There were 63 deaths among the 638 patients (9.9%). 32 (51%) of the deaths were attributed mainly to COPD. Patients with higher proadrenomedullin values were at higher risk for death ($p<0.0001$). In the multivariate analysis, proadrenomedullin HR (95% CI) 1.83 (1.34-2.51, p=0.0002), BMI 0.48 (0.32-0.72, p=0.0004) and 6 MWD 0.6 (0.4-0.91, p=0.0152) but not MMRC 1.31 (0.94-1.84, p=0.113) and FEV1%pred 1.17 (0.68-2, p=0.5727) were significantly associated with 2 year survival. The C-index for the prediction of mortality in the Cox-regression analysis was 0.676 for the BODE index and 0.658 for proadrenomedullin ($p<0.0001$ both). The addition of proadrenomedullin to the BODE index improved its performance significantly (C-index 0.743, p=0.00020). In combination with proadrenomedullin, the BMI (B), the degree of airflow obstruction (O) and dyspnea (D) domains by itself (e.g. without exercise capacity) performed similarly to the BODE index (C-index 0.772).
Conclusion: Proadrenomedullin improves the performance of the BODE index at predicting the risk of death from any cause among patients with COPD.

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Is the bacterium Tropheryma whipplei cause of the disease in a subgroup of patients with presumed sarcoidosis?

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Introduction: Recently we published a case report presenting a patient in whom a causal relationship between pulmonary sarcoidosis and infection with Tropheryma whipplei (T. whipplei) could be demonstrated1. To our best knowledge this is the first systematic study investigating the hypothesis, that in a subgroup of patients presumed sarcoidosis is caused by T. whipplei.
Patients and methods: A total of 56 consecutive patients in whom a diagnosis of sarcoidosis was suspected clinically and confirmed histologically were included in this retrospective study (m:f = 21:35, mean age$\pm$SD = 53.6$\pm$16.2 (range 24–90 years).
PCR-examination for T. whipplei was performed in all patients, using formalin-fixed and paraffin-embedded specimens obtained from organs affected by sarcoidosis [lung (n=22), lymph nodes (n=15), skin (n=7), liver (n=6), other organs (n=6)]. All PCR-examinations were done in an international reference laboratory for Whipple's disease.
Results: T. whipplei-RNA was detected in tissues affected by sarcoidosis in 2 of 56 patients (3.6%). Both patients were women (age: 32 and 85 years, respectively) and had enlarged mediastinal and hilar lymph nodes. Histological examination of affected lymph nodes showed granulomatous lymphadenitis of sarcoid type, PAS-staining was negative. Both patients had no gastrointestinal symptoms. Further evaluation for the presence of Whipple's disease is ongoing.
Conclusion: Our findings contribute further evidence to the hypothesis, that in a subgroup of patients presumed sarcoidosis is caused by infection with the bacterium T. whipplei. However, this hypothesis should be further evaluated in prospective studies.
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Sarcoidosis relapses in corticosteroid treated patients

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Aim: Assessing the frequency of relapses and the disease characteristics associated with relapses in corticosteroid treated sarcoidosis patients.
Subjects and methods: 125 patients with biopsy-proven sarcoidosis treated with corticosteroids for 6-18 months after diagnosis were evaluated. Number and type of relapses were noted during the follow-up period. The clinical and laboratory parameters were compared in patients with a relapse of the disease versus (vs) patients without relapses.
Results: 38 patients (30%) had a sarcoidosis relapse, 2-42 months after the treatment stop (mean interval 11$\pm$13 months). The manifestations were clinical in 36 patients (similar symptoms as at diagnosis), radiological in 34 and functional in 26 (decreased diffusion capacity in 22 patients, pulmonary volumes in 13 and flows in 15).
The relapses were seen in 7 patients with complete remission after the first treatment, 30 with partial remission and 1 with stationary evolution.
The patients with relapses had more frequent interstitial lung disease at diagnosis compared to patients without relapses (88 vs 59%, p=0.007), more frequent duration <1 year of the first treatment (42 vs 10%, p=0.007), more severe diffusion capacity impairment (26 vs 10%, p=0.044) or absence of complete remission after the first treatment (81 vs 45%, p=0.003). No other significant differences were seen in clinical or laboratory parameters.
Conclusions: Almost one third of the sarcoidosis patients in which corticosteroid treatment was necessary at diagnosis had a disease relapse during the follow-up period. Disease severity at diagnosis or at the end of the first corticosteroid treatment and the short duration of the treatment were associated with the occurrence of a relapse.

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Occurrence of hypersensitivity to beryllium among patients with diagnosed sarcoidosis. Initial results

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Introduction: Sarcoidosis is a form of interstitial lung disease of unknown cause. In this disease the formations of granulomas are diagnosed also among individuals with berylliosis – an occupational disease clinically similar to sarcoidosis, but associated with hypersensitivity to beryllium.
Aim of study: Our objective is to determine the frequency of hypersensitivity to beryllium in individuals with diagnosed sarcoidosis of lungs and to attempt to work out diagnostic methods of berylliosis.
Methodology: Individuals selected for the research were diagnosed with sarcoidosis. All individuals were screened using a modified beryllium lymphocyte proliferation test (BeLPT). The method involved isolating blood lymphocytes, staining them with fluorescent marker (CFSE) and exposing them to beryllium sulfate (of various concentration) or mitogen (positive control). The number of dividing cells (CFSE dilution) was marked after 5 days of incubation with flow cytometry. Individuals suspected of positive proliferation test result and those suspected of the risk for beryllium compounds exposure will be examined by patch tests with beryllium sulfate.
Results: 30 individuals with sarcoidosis have been tested. 5 of them (14.3%) exhibited increased lymphocyte proliferation index.
Conclusions: The study attempts to present a new diagnostic method of identifying hypersensitivity to beryllium. Presently, neither reliable in vitro tests for berylliosis have been standardised nor routinely carried out. Our method requires validation among patients with berylliosis, testing the method in control group and comparison of BeLPT-CFSE methods with a standard thymidine test.

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Pentraxin-3: A novel biomarker for the differentiation of parapneumonic effusion and malignant pleural effusion

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Pentraxin-3(PTX-3) is a new marker of inflammation. Pentraxins like C-reactive protein are key components of the innate immune system. Diagnostic value of PTX-3 in parapneumonic pleural effusion (PPPE) and malign pleural effusion(MPE) has not been examined before.
The concentrations of pleural fluid PTX-3 were measured in a total of 61 patients: 20 with PPPE and 41 with MPE. A diagnosis PPPE was based upon the presence of an effusion in patients with clinical and radiological evidence of acute pneumonia. A malignant pleural effusion(PE) was defined by pleural biopsy or the presence of malignant cells on PE cytology. The area under the curve (AUC) quantified the overall diagnostic accuracy of the tests.
The study demonstrated that PTX-3 concentration was higher in pleural fluid of PPPE patients compared with MPE patients (31.8 ng/mL vs 6.9 ng/mL, respectively, $p<0.001$). Pleural effusion PTX-3 demonstrated AUCs of 0.802 (95% CI: 0.683–0.921, $P<0.001$) for diagnosing effusions due to PPPE. The sensitivity and specificity of PE-PTX-3 for PPPE at the cut-off concentration of 8.5 ng/mL was 80% and 64%, respectively.
Measuring PTX-3 concentrations in pleural fluid may be helpful in distinguishing pleural effusion due to a PPPE or MPE aetiology.

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Diagnostic accuracy of pleural fluid NTpro-BNP for pleural effusions of cardiac origin

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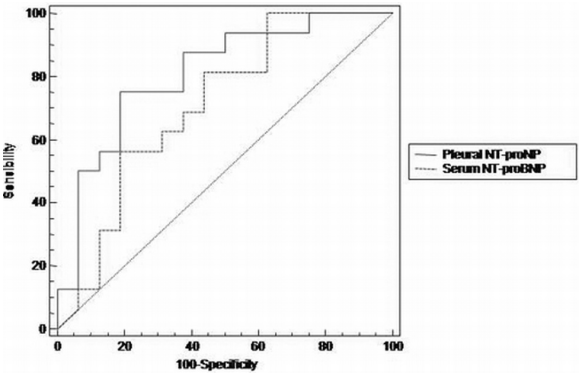
Introduction: The most frequent cause of a pleural effusion is heart failure. The diagnosis is based on clinical findings and biochemical parameters.
Rationale: The existence of a specific heart biomarker could avoid unnecessary studies for the diagnosis of cardiac origin of pleural fluids.
Objective: The purpose of our study was to evaluate the diagnostic accuracy of pleural fluid aminoterminal fragment N-terminal pro-brain natriurético peptide (NTpro-BNP) for pleural effusions of cardiac origin compared with Framingham criteria.
Material and methods: We studied 32 consecutive patients admitted at the work site. Pleural and blood samples were simultaneously obtained
NTpro-BNP was measured in blood and pleural fluids (Bio Merieux® Enzyme-Linked Fluorescent Assay). Light criteria and serum-pleural albumin gradient was used to discriminate transudates from exudates.
Results: The cut-off value of pleural fluid NTpro-BNP level to discriminate between pleural effusions due to heart failure was ≥1.791 pg/mL. The sensitivity and specificity was 75.0%(95%CI 47.6-92.6) and 81.2%(95%CI 54.4-95.7) respectively; with a positive predictive value of 80.0%(95%CI 51.9-96.0), negative predictive value 81.8%(95%CI 50.1-93.2), positive likelihood ratio 4.0(95%CI 20.8-5.8) and negative likelihood ratio 0.3(95%CI 0.1-1.2).



Conclusions: Pleural fluid NTpro-BNP is a very useful biomarker with high diagnostic accuracy for distinguishing pleural effusions of cardiac origin.