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Abstracts' Service

Feasibility and Safety of Outpatient Medical Thoracoscopy at a Large Tertiary Medical Center: A Collaborative Medical-Surgical Initiative

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Background. Medical thoracoscopy (MT) is performed by relatively few pulmonologists in the United States. Recognizing that an outpatient minimally invasive procedure such as MT could provide a suitable alternative to hospitalization and surgery in patients with undiagnosed exudative pleural effusions, we initiated the Mayo Clinic outpatient MT program and herein report preliminary data on safety, feasibility, and outcomes.

Methods. All consecutive patients referred for outpatient MT from October 2011 to August 2013 were included in this study. Demographic, radiographic, procedural, and histologic data were recorded prospectively and subsequently analyzed.

Results. Outpatient MT was performed on 51 patients, with the most common indication being an undiagnosed lymphocytic exudative effusion in 86.3% of the cohort. Endoscopic findings included diffuse parietal pleural inflammation in 26 patients (51%), parietal pleural studding in 19 patients (37.3%), a normal examination in three patients (5.9%), diffuse parietal pleural thickening in two patients (3.9%), and a diaphragmatic defect in one patient (2%). Pleural malignancy was the most common histologic diagnosis in 24 patients (47.1%) and composed predominantly of mesothelioma in 14 (27.5%). Nonspecific pleuritis was the second most frequent diagnosis in 23 patients (45.1%). There were very few complications, with no significant cases of hemodynamic or respiratory compromise and no deaths.

Conclusions. Outpatient MT can be integrated successfully into a busy tertiary referral medical center through the combined efforts of interventional pulmonologists and thoracic surgeons. Outpatient MT may provide patients with a more convenient alternative to an inpatient surgical approach in the diagnosis of undiagnosed exudative pleural effusions while maintaining a high diagnostic yield and excellent safety.

Efficacy and Safety of Early Dexmedetomidine During Noninvasive Ventilation for Patients with Acute Respiratory Failure: Randomized, Double-Blind, Placebo-Controlled Pilot Study

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Background. Successful application of noninvasive ventilation (NIV) for acute respiratory failure (ARF) requires patient cooperation and comfort. The efficacy and safety of early IV dexmedetomidine when added to protocolized, as-needed IV midazolam and fentanyl remain unclear.

Methods. Adults with ARF and within 8 h of starting NIV were randomized to receive IV dexmedetomidine (0.2 μg/kg/h titrated every 30 min to 0.7 μg/kg/h to maintain a Sedation-Agitation Scale [SAS] score of 3 to 4) or placebo in a double-blind fashion up to 72 h, until NIV was stopped for ≥ 2 h, or until intubation. Patients with agitation (SAS ≥ 5) or pain (visual analog scale ≥ 5 of 10 cm) 15 min after each dexmedetomidine and placebo increase could receive IV midazolam 0.5 to 1.0 mg or IV fentanyl 25 to 50 μg, respectively, at a minimum interval of every 3 h.

Results. The dexmedetomidine (n = 16) and placebo (n = 17) groups were similar at baseline. Use of early dexmedetomidine did not improve NIV tolerance (score, 1 of 4; OR, 1.44; 95% CI, 0.44-4.70; P = .54) nor, vs placebo, led to a greater median (interquartile range) percent time either tolerating NIV (99% [61%-100%] vs 67% [40%-100%], P = .56) or remaining at the desired sedation level (SAS score = 3 or 4, 100% [86%-100%] vs 100% [100%-100%], P = .28], or fewer intubations (P = .79). Although use of dexmedetomidine was associated with a greater duration of NIV vs placebo

(37 [16-72] vs 12 [4-22] h, P = .03), the total ventilation duration (NIV + invasive) was similar (3.3 [2-4] days vs 3.8 [2-5] days, P = .52). More patients receiving dexmedetomidine had one or more episodes of deep sedation vs placebo (SAS ≤ 2, 25% vs 0%, P = .04). Use of midazolam (P = .40) and episodes of either severe bradycardia (heart rate ≤ 50 beats / min, P = .18) or hypotension (systolic BP ≤ 90 mm Hg, P = .64) were similar.

Conclusions. Initiating dexmedetomidine soon after NIV initiation in patients with ARF neither improves NIV tolerance nor helps to maintain sedation at a desired goal. Randomized, multicenter trials targeting patients with initial intolerance are needed to further elucidate the role for dexmedetomidine in this population.

Trial registry: ClinicalTrials.gov; No: NCT00871624; URL: www.clinicaltrials.gov

Do Grandmaternal Smoking Patterns Influence the Etiology of Childhood Asthma?

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Background. Animal data suggest that tobacco smoke exposure of a mother when she is in utero influences DNA methylation patterns in her offspring and that there is an effect on the respiratory system, particularly airway responsiveness. The only study, to our knowledge, in humans suggests that there is a similar effect on asthma. The present study tests whether an association with respiratory problems can be confirmed in a large population study and aims to determine whether in utero exposure of the father has similar effects on his offspring.

Methods. Information from the Avon Longitudinal Study of Parents and Children was used to compare the offspring of women and of men who had themselves been exposed to cigarette smoke in utero; separate analyses were performed for children of women smokers and nonsmokers. The outcome measures were trajectories of history of early wheezing, doctor-diagnosed asthma by age 7 years, and results of lung function and methacholine challenge tests at 8 years. A variety of social and environmental factors were taken into account; offspring sexes were examined separately.

Results. There was no association with any outcome in relation to maternal prenatal exposure. There was some evidence of an increase in asthma risk with paternal prenatal exposure when the study mother was a nonsmoker (adjusted OR, 1.17; 95% CI, 0.97-1.41). This was particularly strong for girls (adjusted OR, 1.39; 95% CI, 1.04-1.86).

Conclusions. We did not find that maternal prenatal exposure to her mother's smoking had any effect on her children's respiratory outcomes. There was suggestive evidence of paternal prenatal exposure being associated with asthma and persistent wheezing in the granddaughters.

Comparison of Gastroesophageal Reflux Disease Questionnaire and Multichannel Intraluminal Impedance pH Monitoring in Identifying Patients With Chronic Cough Responsive to Antireflux Therapy

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Background. Empirical therapy has been recommended as an initial clinical approach for treating gastroesophageal reflux-induced chronic cough (GERC). This study compared the predictive accuracy of the Gastroesophageal Reflux Disease Questionnaire (GerdQ) with the accuracy of multichannel intraluminal impedance pH monitoring (MII-pH) for GERC.

Methods. A total of 126 consecutive patients with potential GERC were recruited to undergo MII-pH and complete the GerdQ. A final diagnosis of GERC was made after favorable response to consequent medicinal antireflux therapy, regardless of laboratory findings. The predictive accuracy of the GerdQ for GERC was assessed and compared with that of MII-pH.

Results. GERC was confirmed in 102 of 126 patients (81.0%); cough was due to acid reflux in 55 (53.9%) and nonacid reflux in 47 (46.1%). The optimal cutoff point of the GerdQ for predicting GERC was defined as 8.0 according to the highest Youden index of 0.584, with a sensitivity of 66.7%, specificity of 91.7%, positive predictive value of 97.1%, and negative predictive value of 42.9%. A subanalysis for only acid GERC showed further improvement in the predictive accuracy of the GerdQ, corresponding to a sensitivity of 90.9%, specificity of 78.6%, positive predictive value of 71.4%,

and negative predictive value of 96.4%. However, a meaningful GerdQ cutoff point for prediction of nonacid GERC could not be determined. In general, MII-pH was superior to the GerdQ for predicting GERC and acid GERC.

Conclusions. The GerdQ can be used for predicting acid GERC but not nonacid GERC and is inferior to MII-pH.

Trial registry. Chinese Clinical Trial Registry; No.: ChiCTR-ODT-12001899; URL: www.chictr.org

Attendance at Pulmonary Rehabilitation Classes: An Exploration of Demographic, Physiological and Psychological Factors that Predict Completion of Treatment

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Pulmonary rehabilitation (PR) is an effective treatment for people with chronic obstructive pulmonary disease (COPD). However, uptake and adherence to rehabilitation is poor and non-adherence is associated with poorer clinical outcomes. This study investigated the factors that might predict an individual completing his/her PR programme. Demographic, physiological and psychological data were collected from routine assessment information. Non-completers (N = 213) who dropped out after initial assessment were compared with completers (N = 438) who attended all 6 weeks of PR programme. Regression analysis indicated that smoking status was the strongest predictor for completing PR programme, that is, ex-smokers were 2.6 times (95% confidence interval (CI) = 1.7–3.9) and those who had never smoked were 2.5 times (95% confidence interval (CI) = 1.1–5.7) more likely to complete in comparison with those who were current smokers. Scoring better on psychological well-being measures (odds ratio = 1.6; 95% CI = 1.2–1.9) was also a strong predictor. The findings suggest the areas that could be addressed to enhance adherence to rehabilitation, for example, targeted interventions for clients who continue to smoke and for those who require support for psychological distress.

Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD

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Background. Treatment with inhaled glucocorticoids in combination with long-acting bronchodilators is recommended in patients with frequent exacerbations of severe chronic obstructive pulmonary disease (COPD). However, the benefit of inhaled glucocorticoids in addition to two long-acting bronchodilators has not been fully explored.

Methods. In this 12-month, double-blind, parallel-group study, 2485 patients with a history of exacerbation of COPD received triple therapy consisting of tiotropium (at a dose of 18 µg once daily), salmeterol (50 µg twice daily), and the inhaled glucocorticoid fluticasone propionate (500 µg twice daily) during a 6-week run-in period. Patients were then randomly assigned to continued triple therapy or withdrawal of fluticasone in three steps over a 12-week period. The primary end point was the time to the first moderate or severe COPD exacerbation. Spirometric findings, health status, and dyspnea were also monitored.

Results. As compared with continued glucocorticoid use, glucocorticoid withdrawal met the prespecified noninferiority criterion of 1.20 for the upper limit of the 95% confidence interval (CI) with respect to the first moderate or severe COPD exacerbation (hazard ratio, 1.06; 95% CI, 0.94 to 1.19). At week 18, when glucocorticoid withdrawal was complete, the adjusted mean reduction from baseline in the trough forced expiratory volume in 1 second was 38 ml greater in the glucocorticoid-withdrawal group than in the glucocorticoid-continuation group (P<0.001); a similar between-group difference (43 ml) was seen at week 52 (P=0.001). No change in dyspnea and minor changes in health status occurred in the glucocorticoid-withdrawal group.

Conclusions. In patients with severe COPD receiving tiotropium plus salmeterol, the risk of moderate or severe exacerbations was similar among those who discontinued inhaled glucocorticoids and those who continued glucocorticoid therapy. However, there was a greater decrease in lung function during the final step of glucocorticoid withdrawal.

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Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma

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Background. Many patients with severe asthma require regular treatment with oral glucocorticoids despite the use of high-dose inhaled therapy. However, the regular use of systemic glucocorticoids can result in serious and often irreversible adverse effects. Mepolizumab, a humanized monoclonal antibody that binds to and inactivates interleukin-5, has been shown to reduce asthma exacerbations in patients with severe eosinophilic asthma.

Methods. In a randomized, double-blind trial involving 135 patients with severe eosinophilic asthma, we compared the glucocorticoid-sparing effect of mepolizumab (at a dose of 100 mg) with that of placebo administered subcutaneously every 4 weeks for 20 weeks. The primary outcome was the degree of reduction in the glucocorticoid dose (90 to 100% reduction, 75 to less than 90% reduction, 50 to less than 75% reduction, more than 0 to less than 50% reduction, or no decrease in oral glucocorticoid dose, a lack of asthma control during weeks 20 to 24, or withdrawal from treatment). Other outcomes included the rate of asthma exacerbations, asthma control, and safety.

Results. The likelihood of a reduction in the glucocorticoid-dose stratum was 2.39 times greater in the mepolizumab group than in the placebo group (95% confidence interval, 1.25 to 4.56; P=0.008). The median percentage reduction from baseline in the glucocorticoid dose was 50% in the mepolizumab group, as compared with no reduction in the placebo group (P=0.007). Despite receiving a reduced glucocorticoid dose, patients in the mepolizumab group, as compared with those in the placebo group, had a relative reduction of 32% in the annualized rate of exacerbations (1.44 vs. 2.12, P=0.04) and a reduction of 0.52 points with respect to asthma symptoms (P=0.004), as measured on the Asthma Control Questionnaire 5 (in which the minimal clinically important difference is 0.5 points). The safety profile of mepolizumab was similar to that of placebo.

Conclusions. In patients requiring daily oral glucocorticoid therapy to maintain asthma control, mepolizumab had a significant glucocorticoid-sparing effect, reduced exacerbations, and improved control of asthma symptoms.

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