DETECTING LUNG CANCER USING EXHALED BREATH ANALYSIS

Volatile organic compounds (VOC) in the breath have been identified as potential biomarkers of lung cancer. Phillips and colleagues (J Breath Res 2019;13:036013) investigated whether a breath VOC biomarker of lung cancer could also predict pulmonary nodules on low-dose chest CT (LDCT). The study enrolled patients undergoing LDCT screening for lung cancer. The initial phase employed an unblinded analysis of the exhaled breath of 301 subjects. Analysis identified a mass ion biomarker, termed mass abnormalities in gaseous ions with imaging correlates (MAGIIC). Cross-referencing with a library of mass spectra, it appeared MAGIIC may be related to metabolic products of oxidative stress. Subsequent blinded validation in a separate group of 161 lung cancer screening participants demonstrated optimum sensitivity and specificity for biopsy-proven lung cancer of 75% and 85%, respectively. Accuracy for pulmonary nodules was 77% and 81%, based on analysis from two separate laboratories. The level of MAGIIC in breath was not significantly affected by smoking history. MAGIIC and other similar biomarkers may be useful as a supplement to LDCT to assess the likelihood that a pulmonary nodule is malignant.

TALC POUDRAGE OR SLURRY FOR INITIAL MANAGEMENT OF MALIGNANT PLEURAL EFFUSION

Talc pleurodesis is a common intervention for malignant pleural effusions (MPE), however, the optimal methods for talc delivery are unknown. Bhatnagar *et al* (JAMA 2020;323:600) present a prospective open-label randomised controlled trial comparing whether administration of talc poudrage during medical thoracoscopy, using light sedation as opposed to a general anaesthetic, was more effective than talc slurry delivered via chest tube. Recruitment lasted 6 years from August 2012 to April 2018, randomising 330 participants (mean age, 68 years; 181 (55%) women). Eligibility criteria were ≥ 18 years old, a confirmed diagnosis of MPE and ability to undergo medical thoracoscopy. Exclusion criteria

were evidence of non-expandable lung or those requiring a diagnostic thoracoscopy. Patients in the talc poudrage group ($n=166$) received 4g of talc poudrage during thoracoscopy, while patients in the control group ($n=164$) underwent bedside chest tube insertion and administration of 4g of sterile talc slurry. The primary outcome analysis, treatment failure at 90 days, revealed no significant difference between the two treatment arms. The pleurodesis failure rate was 36 of 161 patients (22%) in the talc poudrage group and 38 of 159 (24%) in the talc slurry group (adjusted OR 0.91, 95% CI 0.54 to 1.55; $p=0.74$). No statistically significant differences were noted in any of the 24 prespecified secondary outcomes (such as all-cause mortality, length of inpatient stay and reported pain). Clinicians can be reassured that method of talc delivery does not materially impact treatment efficacy and so can choose the most appropriate option based on patient preference, local care pathways and clinical experience.

IMPACT OF ACYCLOVIR USE ON SURVIVAL OF PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA AND HIGH-LOAD HERPES SIMPLEX VIRUS REPLICATION

While herpes simplex virus (HSV) replication is present in the respiratory secretions of many ventilated intensive care unit (ICU) patients, the clinical significance remains unclear. Schuier and colleagues (Critical Care 2020;24:12) conducted a retrospective analysis of patients with ventilator-associated pneumonia and HSV testing of their respiratory secretions. Respiratory secretions (bronchoalveolar lavage fluid or tracheal aspirates) were assessed for HSV replication by PCR analysis. Clinical parameters, and radiographic findings and ICU survival times were retrospectively compared between acyclovir-treated and untreated patients with high ($>10^5$ HSV copies/mL) and low (10^3 – 10^5 HSV copies/mL) viral load. Initially, 125 patients were identified with subsequent exclusion of 36 patients with underlying immunosuppression, without clinical features of pneumonia or with a good clinical response to antibiotic therapy. Fewer patients with high viral load responded to antibiotics (12% vs 40%, $p=0.001$). Of the remaining 89 patients, 30 had low (16 treated with acyclovir) and 59 high (49 treated) viral loads. Acyclovir improved median ICU survival (8 days vs 22 days, $p=0.014$), and the HR for ICU

death was significantly reduced (HR=0.31, 95% CI 0.11 to 0.92, $p=0.035$) in high-load patients. Moreover, circulatory and pulmonary oxygenation function of high-load patients improved significantly with reduced inotrope requirements ($p=0.049$), improved gas exchange and chest radiographic findings ($p<0.001$). An attempt to mitigate for the trial design was performed with a propensity score-matched analysis which indicated similar results. The authors concluded, in patients with ventilator-associated pneumonia, antibiotic treatment failure and high levels of HSV replication, acyclovir treatment should be considered.

EXPIRATORY FLOW LIMITATION MAY HIGHLIGHT THOSE AT RISK OF LOSS OF EXERCISE CAPACITY FOLLOWING COMPLETION OF PULMONARY REHABILITATION

The benefits of pulmonary rehabilitation (PR) for COPD are well established. However, it is resource intense and individual response varies. Zimmerman *et al*'s (IJ COPD 2020;15:157) pilot observational study investigated if baseline force oscillation technique (FOT) parameters relate to changes in exercise capacity in patients with COPD following PR. Fifteen participants (age 75 ± 6 years, FEV_1 1.44 ± 0.48 L) had FOT, spirometry and 6 min walk distance (6MWD) performed before PR, immediately after PR and 3 months after PR. Expiratory flow limitation (EFL), measured by FOT and defined by change in respiratory system reactance (ΔX_{rs}), correlated with quality of life assessed with St George questionnaire ($rs=0.80$, $p<0.01$). While baseline FOT parameters did not predict improvement in 6MWD following PR, there was an association with maintenance of improvement in the subsequent 3 months (ΔX_{rs} baseline to change in 6MWD end of PR to 3 months after PR: $rs=-0.65$, $p=0.02$). The investigators concluded that baseline EFL may help predict those patients with COPD most at risk of loss of exercise capacity following completion of PR, allowing targeted intervention such as repeat or maintenance programmes.

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