

Abstracts' Service

Adult Bronchoscopy Training: Current State and Suggestions for the Future: CHEST Expert Panel Report

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Background. The determination of competency of trainees in programs performing bronchoscopy is quite variable. Some programs provide didactic lectures with hands-on supervision, other programs incorporate advanced simulation centers, whereas others have a checklist approach. Although no single method has been proven best, the variability alone suggests that outcomes are variable. Program directors and certifying bodies need guidance to create standards for training programs. Little well-developed literature on the topic exists.

Methods. To provide credible and trustworthy guidance, rigorous methodology has been applied to create this bronchoscopy consensus training statement. All panelists were vetted and approved by the CHEST Guidelines Oversight Committee. Each topic group drafted questions in a PICO (population, intervention, comparator, outcome) format. MEDLINE data through PubMed and the Cochrane Library were systematically searched. Manual searches also supplemented the searches. All gathered references were screened for consideration based on inclusion criteria, and all statements were designated as an Ungraded Consensus-Based Statement.

Results. We suggest that professional societies move from a volume-based certification system to skill acquisition and knowledge-based competency assessment for trainees. Bronchoscopy training programs should incorporate multiple tools, including simulation. We suggest that ongoing quality and process improvement systems be introduced and that certifying agencies move from a volume-based certification system to skill acquisition and knowledge-based competency assessment for trainees. We also suggest that assessment of skill maintenance and improvement in practice be evaluated regularly with ongoing quality and process improvement systems after initial skill acquisition.

Conclusions. The current methods used for bronchoscopy competency in training programs are variable. We suggest that professional societies and certifying agencies move from a volume-based certification system to a standardized skill acquisition and knowledge-based competency assessment for pulmonary and thoracic surgery trainees.

A Novel Method for In Vivo Imaging of Solitary Lung Nodules Using Navigational Bronchoscopy and Confocal Laser Microendoscopy

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Solitary pulmonary nodules (SPN) have become increasingly prevalent and diagnostic management remains challenging. We demonstrate a novel technique in which probe-based confocal endomicroscopy (pCLE) could be performed to microimage SPN in vivo and in real-time. Two confocal wavelengths (488 and 660 nm with methylene blue (MB)) were used for elastin network and cellular imaging, respectively using pCLE in conjunction with r-EBUS and virtual navigation. In the first case, the 1-mm Alveoflex was used to

image a metastatic melanoma in a subcentimetric nodule in the right middle lobe. In the next case, a malignant 2-cm nodule in the posterior segment of the upper lobe was imaged using the smaller 0.6-mm Cholangioflex. Lastly, we present a benign case revealing confocal characteristics of a nodular lipid pneumonitis. This reports for the first time the feasibility and utility of pCLE in vivo microimaging of SPN using either the Alveoflex or Cholangioflex miniprobes in addition to 660 nm/MB imaging.

A Bronchial Genomic Classifier for the Diagnostic Evaluation of Lung Cancer

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Background. Bronchoscopy is frequently nondiagnostic in patients with pulmonary lesions suspected to be lung cancer. This often results in additional invasive testing, although many lesions are benign. We sought to validate a bronchial-airway gene-expression classifier that could improve the diagnostic performance of bronchoscopy.

Methods. Current or former smokers undergoing bronchoscopy for suspected lung cancer were enrolled at 28 centers in two multicenter prospective studies (AEGIS-1 and AEGIS-2). A gene-expression classifier was measured in epithelial cells collected from the normal-appearing mainstem bronchus to assess the probability of lung cancer.

Results. A total of 639 patients in AEGIS-1 (298 patients) and AEGIS-2 (341 patients) met the criteria for inclusion. A total of 43% of bronchoscopic examinations were nondiagnostic for lung cancer, and invasive procedures were performed after bronchoscopy in 35% of patients with benign lesions. In AEGIS-1, the classifier had an area under the receiver-operating-characteristic curve (AUC) of 0.78

(95% confidence interval [CI], 0.73 to 0.83), a sensitivity of 88% (95% CI, 83 to 92), and a specificity of 47% (95% CI, 37 to 58). In AEGIS-2, the classifier had an AUC of 0.74 (95% CI, 0.68 to 0.80), a sensitivity of 89% (95% CI, 84 to 92), and a specificity of 47% (95% CI, 36 to 59). The combination of the classifier plus bronchoscopy had a sensitivity of 96% (95% CI, 93 to 98) in AEGIS-1 and 98% (95% CI, 96 to 99) in AEGIS-2, independent of lesion size and location. In 101 patients with an intermediate pretest probability of cancer, the negative predictive value of the classifier was 91% (95% CI, 75 to 98) among patients with a nondiagnostic bronchoscopic examination.

Conclusions. The gene-expression classifier improved the diagnostic performance of bronchoscopy for the detection of lung cancer. In intermediate-risk patients with a nondiagnostic bronchoscopic examination, a negative classifier score provides support for a more conservative diagnostic approach. (Funded by Allegro Diagnostics and others; AEGIS-1 and AEGIS-2 ClinicalTrials.gov numbers, NCT01309087 and NCT00746759.)

Lung Ultrasound in the Diagnosis and Monitoring of Community Acquired Pneumonia in Children

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Lung ultrasound (LUS) is as an easily accessible, radiation-free imaging technique that might be used as a diagnostic tool in community-acquired pneumonia (CAP).

The aim of the study was to evaluate the usefulness and accuracy of LUS in the diagnosis and monitoring of childhood CAP.

One hundred six consecutive children aged between 1 and 213 (median 52.5) months referred to the hospital with suspicion of CAP were enrolled. All patients underwent LUS on the day of admission, followed by chest radiograph (CXR). Lung ultrasound was also performed in 25 children between 5th-7th and 31 children between 10th-14th day after admission.

Radiographic signs of pneumonia were demonstrated in 76 children, while lung ultrasound revealed pulmonary abnormalities consistent with pneumonia

in 71 children. LUS gave false negative results in 5 patients with parahilar pulmonary infiltrates demonstrated by CXR. Almost perfect overall agreement between LUS and CXR was found in terms of pneumonia diagnosis (Cohen kappa coefficient of 0.89). The diagnostic performance of LUS in demonstration of lung involvement was as follows: sensitivity of 93.4%, specificity of 100%, positive predictive value of 100%, negative predictive value of 85.7% and accuracy of 95.3%.

Our study showed that LUS is a sensitive and highly specific diagnostic method in children with CAP.

Therefore, LUS may be considered as the first imaging test in children with suspicion of CAP. A diagnostic algorithm of CAP which includes LUS should be validated in prospective studies. Lung ultrasound can also be used to follow-up resolution of pneumonic lesions.

Effects of Sigh on Regional Lung Strain and Ventilation Heterogeneity in Acute Respiratory Failure Patients Undergoing Assisted Mechanical Ventilation

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Objective. In acute respiratory failure patients undergoing pressure support ventilation, a short cyclic recruitment maneuver (Sigh) might induce re-aeration of collapsed lung regions, possibly decreasing regional lung strain and improving the homogeneity of ventilation distribution. We aimed to describe the regional effects of different Sigh rates on re-aeration, strain, and ventilation heterogeneity, as measured by thoracic electrical impedance tomography.

Design. Prospective, randomized, cross-over study.

Setting. General ICU of a single university-affiliated hospital.

Patients. We enrolled 20 critically ill patients intubated and mechanically ventilated with PaO₂/FIO₂ up to 300 mm Hg and positive end-expiratory pressure at least 5 cm H₂O (15 with acute respiratory distress syndrome), undergoing pressure support ventilation as per clinical decision.

Interventions. Sigh was added to pressure support ventilation as a 35 cm H₂O continuous positive airway pressure period lasting 3-4 seconds at different rates (no-Sigh vs 0.5, 1, and 2 Sigh(s)/min). All study phases were randomly performed and lasted 20 minutes.

Measurements and Main Results. In the last minutes of each phase, we measured arterial blood gases, changes in end-expiratory lung volume of nondependent and dependent regions, tidal volume reaching nondependent and dependent lung (Vt_{nondep} and Vt_{dep}), dynamic intratidal ventilation heterogeneity, defined as the average ratio of Vt reaching nondependent/Vt reaching dependent lung regions along inspiration (VtH_{it}). With Sigh, oxygenation improved ($p < 0.001$ versus no-Sigh), end-expiratory lung volume of nondependent and dependent regions increased ($p < 0.01$ versus no-Sigh), Vt_{nondep} showed a trend to reduction, and Vt_{dep} significantly decreased ($p = 0.11$ and $p < 0.01$ vs no-Sigh, respectively). VtH_{it} decreased only when Sigh was delivered at 0.5/min ($p < 0.05$ versus no-Sigh), while it did not vary during the other two phases.

Conclusions. Sigh decreases regional lung strain and intratidal ventilation heterogeneity. Our study generates the hypothesis that in ventilated acute respiratory failure patients, Sigh may enhance regional lung protection.

Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer

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Background. Patients with advanced squamous-cell non-small-cell lung cancer (NSCLC) who have disease progression during or after first-line chemotherapy have limited treatment options. This randomized, open-label, international, phase 3 study evaluated the efficacy and safety of nivolumab, a fully human IgG4 programmed death 1 (PD-1) immune-checkpoint-inhibitor antibody, as compared with docetaxel in this patient population.

Methods. We randomly assigned 272 patients to receive nivolumab, at a dose of 3 mg per kilogram of

body weight every 2 weeks, or docetaxel, at a dose of 75 mg per square meter of body-surface area every 3 weeks. The primary end point was overall survival.

Results. The median overall survival was 9.2 months (95% confidence interval [CI], 7.3 to 13.3) with nivolumab versus 6.0 months (95% CI, 5.1 to 7.3) with docetaxel. The risk of death was 41% lower with nivolumab than with docetaxel (hazard ratio, 0.59; 95% CI, 0.44 to 0.79; $P < 0.001$). At 1 year, the overall survival rate was 42% (95% CI, 34 to 50) with nivolumab versus 24% (95% CI, 17 to 31) with

docetaxel. The response rate was 20% with nivolumab versus 9% with docetaxel ($P=0.008$). The median progression-free survival was 3.5 months with nivolumab versus 2.8 months with docetaxel (hazard ratio for death or disease progression, 0.62; 95% CI, 0.47 to 0.81; $P<0.001$). The expression of the PD-1 ligand (PD-L1) was neither prognostic nor predictive of benefit. Treatment-related adverse events of grade 3 or 4 were reported in 7% of the patients in the

nivolumab group as compared with 55% of those in the docetaxel group.

Conclusions. Among patients with advanced, previously treated squamous-cell NSCLC, overall survival, response rate, and progression-free survival were significantly better with nivolumab than with docetaxel, regardless of PD-L1 expression level. (Funded by Bristol-Myers Squibb; CheckMate 017 ClinicalTrials.gov number, NCT01642004.)