

Hot topics from the Assemblies

Adaptive servo-ventilation for central sleep apnea in systolic heart failure

Authors: Cowie MR, Woehrle H, Wegscheider K, *et al.* *N Engl J Med* 2015; 373: 1095–1105.

Summary: Cowie *et al.* present the results of the international, multicentre, randomised, parallel-group SERVE-HF (Treatment of sleep-disordered breathing with predominant central sleep apnea by adaptive servo ventilation in patients with heart failure) trial, which investigated the effects of adding adaptive servo-ventilation (ASV) to guideline based medical management on survival and cardiovascular outcomes in patients with heart failure defined as reduced ejection fraction (<45%) and predominant central sleep apnoea (CSA).

The primary end-point examined was the time to first event of all-cause death, life-saving cardiovascular intervention, or unplanned hospitalisation for worsening chronic heart failure. There were 1325 patients enrolled in the study with 659 patients randomised to the control group and 666 to the ASV group. The incidence of the primary end-point did not differ between groups (hazard ratio (HR) 1.13, 95% CI 0.97–1.31; $p=0.10$) and there was no beneficial effect on quality-of-life, 6-minute walking distance or symptoms. The study found that ASV treated CSA and daytime sleepiness effectively, but significantly increased cardiovascular mortality (HR 1.34, 95% CI 1.09–1.65; $p=0.006$) and all-cause mortality (HR 1.28, 95% CI 1.06–1.55; $p=0.01$).

These results cannot be generalised to heart failure patients with preserved ejection fraction or predominantly obstructive events. The pathophysiology of the increased cardiovascular mortality associated with this therapy remains to be elucidated.

Reviewed by: Athanasia Panaka (Greece, Assembly 4)

Reduced force of diaphragm muscle fibers in patients with chronic thromboembolic pulmonary hypertension

Authors: Manders E, Bonta PI, Kloek JJ, *et al.*

Am J Physiol Lung Cell Mol Physiol 2016; 311: L20–L28.

Summary: Previous studies have demonstrated an important reduction of maximal inspiratory pressure (MIP) in patients with pulmonary hypertension. MANDERS *et al.* hypothesised that impaired diaphragm muscle fibre contractility could be associated with reduced MIP. They measured the *ex vivo* diaphragm muscle fibre contractility of

13 patients with operable chronic thromboembolic pulmonary hypertension (CTEPH) who underwent pulmonary endarterectomy and compared it to their MIP obtained before surgery. A control group was selected from patients who underwent elective lung cancer resection ($n=15$).

No significant difference in muscle fibre cross sectional area was found between groups. However, the maximal tension of slow-twitch muscle fibres was significantly lower in patients with CTEPH than in controls, possibly because of a reduction in myosin heavy chain concentration. In addition, submaximal tension was reduced in fast-twitch muscle fibres. Importantly, they found an association between maximal force of diaphragm fibres and MIP. Interestingly, the authors present promising results suggesting an improvement of submaximal contractility in fast-twitch muscle fibres with a fast skeletal troponin activator.

From a clinical perspective, inspiratory muscle training may emerge as an attractive therapeutic strategy in patients with CTEPH but this needs to be addressed in future studies.

Reviewed by: Roberta Pulcheri Ramos (Brazil, Assembly 4)

Left adrenal gland analysis in lung cancer patients using the endobronchial ultrasound scope: a feasibility trial

Authors: Crombag LMMJ, Annema JT.

Respiration 2016; 91:235–240.

Summary: Distant metastases have a significant impact on the prognosis and treatment of lung cancer patients, and the adrenal glands are a predilection site.

Sampling of the left adrenal gland (LAG) can be satisfactorily performed by endoscopic ultrasound-fine needle aspiration (EUS-FNA), using a conventional gastrointestinal echo-endoscope. EUS-FNA is a highly accurate method for LAG analysis and has 86% sensitivity for the detection of LAG metastases. However, there is growing evidence that the combined endobronchial and oesophageal staging can be performed using just the endobronchial ultrasound (EBUS) scope (EUS-B), introducing it into the oesophagus following the endobronchial nodal assessment. In this way, the LAG can also be identified and sampled using an EBUS scope.

The aim of this study was to determine whether the LAG could be identified by EUS-B. 80 consecutive patients received an EUS-B attempt to visualise the LAG. In 68 of them (85% *versus* 97%

Cite as: Hot topics from the Assemblies. *Breathe* 2016; 12: 383–384.



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using the conventional EUS scope) it was feasible to transgastrically identify the LAG. In nine patients, transgastric LAG FNAs were performed. In two cases, the cytopathological evaluation yielded metastases of nonsmall cell lung cancer. The procedure had to be aborted prematurely three times due to vomit reflex and risk of aspiration. No further adverse events were reported and transgastric FNA was uneventful in all patients.

In conclusion, this study highlights that LAG analysis using the EBUS scope is feasible and safe. A single-scope strategy combining complete mediastinal and LAG analysis could provide logistical, practical and financial advantages. Further studies in independent populations are now needed to confirm these findings.

Reviewed by: Simone Scarlata (Italy, Assembly 1)

Hot topics are short (approx. 200 words) summaries of recent important articles in respiratory medicine written by Early Career ERS members. To become a hot topic author, please contact Aran Singanayagam: e-mail: aransinga@gmail.com

Nasopharyngeal microbiota, host transcriptome and disease severity in children with respiratory syncytial virus infection

Authors: de Steenhuijsen Piters WA, Heinonen S, Hasrat R, *et al.*

Am J Respir Crit Care Med 2016; in press [DOI: 10.1164/rccm.201602-0220OC].

Summary: Respiratory syncytial virus (RSV) is the most important infection in infants and results in a wide range of clinical severity. The reasons for this variation are mostly unexplained. In this prospective observational study, the contribution of host nasopharyngeal microbiota to disease

severity related to acute RSV infection was evaluated.

Nasopharyngeal microbiota from 106 patients with RSV (84 hospitalised) and 26 healthy controls were characterised using 16S-rRNA sequencing. Hierarchical clustering analysis demonstrated a predominance of *Haemophilus influenzae* and *Streptococcus pneumoniae* enriched clusters in patients with RSV compared with controls. Non-metric multidimensional scaling analysis revealed a statistically significant positive association between these two clusters and RSV hospitalisation, but an inverse association between *Staphylococcus aureus* and RSV hospitalisation. Analysis of whole blood host transcriptional profiles demonstrated increased modular expression of interferon, Toll-like receptor (TLR) and neutrophil-related genes, including those coding for CD14, TLR4, TLR5, TLR8, interleukin (IL)-6, IL-8 and IL-17A, in RSV patients in the *H. influenzae* and *S. pneumoniae* enriched clusters.

This study highlights an association between increased RSV disease severity and nasopharyngeal colonisation by *H. influenzae* and *S. pneumoniae*. This may be mediated by upregulation of immune-related genes. Given the cross-sectional nature of the study, further work is needed to determine the direction of the cause-effect relationship. These techniques may also hold the key to identifying novel sites of action for treatments or vaccines against RSV infection.

Reviewed by: Holly Emms and Simon B. Drysdale (UK, Assembly 7)