

Hot topics from the Assemblies

Prognostic significance of visceral pleural involvement in early-stage lung cancer

Authors: Lakha S, Gomez JE, Flores RM, *et al.*

Chest 2014; 146: 1619–1626

Summary: The accuracy of non-small cell lung cancer (NSCLC) staging is fundamental for the management of lung cancer patients. Visceral pleural invasion (VPI) is a poor prognostic factor in NSCLC. Its presence results in upstaging of tumours <3 cm according to the American Joint Committee on Cancer (AJCC) TNM staging system. However, the role of VPI as an independent prognostic factor in tumours <7 cm is unclear.

The authors studied the association of VPI with lung cancer-specific (primary outcome) and overall survival (secondary outcome) in 16 315 patients (3389 with VPI) with stage I–II NSCLC treated with lobectomy. The association was assessed with Kaplan–Meier analysis and Cox regression based on data from the Surveillance, Epidemiology and End Results (SEER) registry, a network of US cancer registries.

Worse cancer-specific and overall survival was observed in VPI patients for all tumour sizes ($P < 0.0001$). Cox regression, adjusted for tumour size and other confounders, also showed that VPI was independently associated with decreased lung cancer-specific survival (hazard ratio 1.38; 95% CI 1.29–1.47). Based on these results, the authors created a revised VPI staging classification.

This study demonstrated that VPI is an independent prognostic factor for early stage lung cancer and these findings support the incorporation of the VPI into the staging system for tumors 3–7 cm. This improved classification could lead to better treatment for patients.

Reviewed by: Eleftheria Chaini (Greece, Assembly 11)

Impact of relative contraindications to home management in emergency department patients with low-risk pulmonary embolism

Authors: Vinson DR, Drenten CE, Huang J, *et al.*

Annals ATS 2015; DOI: 10.1513/AnnalsATS.201411-548OC

Summary: The pulmonary embolism (PE) severity index is an internationally recommended prognostic tool for determining 30-day mortality in acute PE. However, factors affecting short-term outcomes and the effect of relative contraindications on the outcome have not yet been determined. In this study, the authors aimed to determine how relative contraindications affect the 5-day and 30-day major outcomes in patients with acute low-risk PE.

Between 2010 and 2012, 423 patients admitted with acute low-risk PE, from four community emergency departments, were retrospectively evaluated. Patients without any relative contraindications were placed in the outpatient-eligible group, and those with at least one relative contraindication were classified as outpatient-ineligible. Relative contraindications were PE-related factors, comorbidities and barriers to treatment adherence or follow-up.

Adverse events within 5 days were recorded in two patients from the outpatient-ineligible group compared

with none in the outpatient-eligible group ($p = 0.13$). The number of patients with major 30-day outcomes was also higher in the outpatient-ineligible group ($n = 9$, 5.9%) than the outpatient-eligible group ($n = 5$, 1.8%) ($p < 0.05$). This study is the first to evaluate the impact of relative contraindications on patients with low-risk PE and showed that most of patients with low-risk acute PE can be treated at home and, for treatment decisions, relative contraindications should be taken into account. Unfortunately, there is still no consensus or definite criteria for determining eligibility for home management. To fully determine the correct indications for how and where to treat low-risk PE patients, more studies are needed.

Reviewed by: Dilek Karadoğan (Turkey, Assembly 6)

Cytisine versus nicotine for smoking cessation

Summary: Walker N, Howe C, Glover M, *et al.*

N Eng J Med 2014; 371: 2353–2362

Summary: Tobacco smoking is the leading preventable cause of mortality. Smoking cessation interventions are highly cost effective in developing countries but the cost of therapies may be prohibitive.

The recent discovery by Walker *et al.* that cytosine is superior to nicotine replacement therapy (NRT) in aiding smoking cessation is welcome as it adds to the paucity of data on a drug used extensively in Eastern Europe for decades. The team conducted an open-label, noninferiority trial that randomised 1310 adult daily smokers to receive cytosine for 25 days or NRT for 8 weeks. At one month, abstinence for smoking was 40% for those receiving cytosine and 31% for those on NRT, a difference of 9.3% (95% CI 4.2–14.5%). The effectiveness of cytosine remained superior at two and six months. Self-reported adverse events were primarily nausea, vomiting and sleep disorders, which were more common in the cytosine group.

The results are of particular relevance to developing countries as it demonstrates the importance of evidence-based research in traditional medicine. It also has value from an economic point of view, as the relatively inexpensive cytosine will ease the pressure on the increasing healthcare budgets of both developing and developed countries. Further research into the cost-effectiveness of cytosine *versus* standard therapy is necessary as it will have profound global clinical and policy implications.

Reviewed by: Helmy Haja Mydin (Malaysia, Assembly 6)

Incidence of viral infection detected by PCR and real-time PCR in childhood community acquired pneumonia: a meta-analysis

Authors: Wang M, Cai F, Wu X, *et al.*

Respirology 2015; 20: 405–412

Summary: Wang *et al.* have conducted a meta-analysis of 21 reports on the incidence of viral childhood community acquired pneumonia (CAP) infection. Studies reporting the incidence of viral infection were analysed, and pooled incidences were calculated with a random-effects model. Subgroup and univariate metaregression analyses were used in exploration of heterogeneity.



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The analysis of 21 eligible reports found that respiratory viruses could be detected in 57.4% (95% CI 50.8–64.1) of paediatric patients with CAP. Of these viral infections, more than half were categorised as mixed infection, with the pooled incidence of 29.3% (95% CI 22.4–36.2). However, it should be highlighted that, first, only 11 out of 21 studies provided raw data to estimate the incidence of mixed infections. Secondly, the heterogeneity was considerable among the pooled incidence estimates of mixed infections. The viruses most frequently detected in childhood CAP were rhinovirus, respiratory syncytial virus and bocavirus. Respiratory viruses were detected at different rates in different patient age groups: 76.1% in those aged ≤ 1 years, 63.1% in those aged 2–5 years and 27.9% in those aged ≥ 6 years.

In conclusion, respiratory viruses were commonly detected by PCR/real-time PCR in paediatric CAP patients with over half also having a concurrent bacterial infection. Reviewed by: Rebecca Huang and Fiona Claxton (UK, Assembly 7)

Semiquantification of pneumothorax volume by lung ultrasound

Authors: Volpicelli G, Boero E, Sverzellati N, *et al.*

Intensive Care Med 2014; 40: 1460–1467

Summary: The clinical utility, reliability and high sensitivity of bedside lung ultrasound (LUS) in the diagnosis of pneumothorax has been widely demonstrated. Despite this, no study has evaluated the possibility of using LUS to estimate pneumothorax volume. Volpicelli *et al.* conducted a prospective, single-blind study to 1) explore the ability of LUS to grade pneumothorax volumes quantified by computed tomography (CT), and 2) to investigate the accuracy of LUS compared with chest radiography (CXR) reading in differentiating small from large pneumothorax. In 124 patients with a diagnosis of pneumothorax of any cause, based on CXR/CT, LUS was performed. The lung point (LP), the projection on the chest wall of the point where visceral and parietal pleura re-adhere and lung sliding reappears, was obtained through LUS and used in subsequent analyses for the quantification of the pneumothorax volume. The LP was proven to be a useful predictor of pneumothorax volume measured by CT. In fact, the lateral progression of the LP corresponded to a progressive increase in pneumothorax volume evaluated with CT. In particular an LP anterior to the mid axillary line was shown to correspond to a lung collapse of 10%, while a LP posterior to the mid-axillary line corresponded to a lung collapse up to 30%. Furthermore, when compared with guidelines criteria based on CXR reading, the LP appeared more accurate and reliable in classifying pneumothorax size. In particular, the

mid-axillary line, which coincided with a 15% lung collapse, represented the most accurate anatomic boundary between large and small pneumothorax. Therefore, an LP located up to this line could suggest a conservative treatment of pneumothorax. For the first time, a study has definitively demonstrated in humans that LUS may be used to reliably grade the size of a pneumothorax. These findings appear to be extraordinarily relevant and could lead to a revolution in the practical management and decision-making process of pneumothorax, considering that LUS is a safe, real-time and radiation-free technique. Reviewed by: Ania Schreiber (Italy, Assembly 2)

Involvement of urokinase in cigarette smoke extract-induced epithelial–mesenchymal transition in human small airway epithelial cells

Authors: Wang Q, Wang Y, Zhang Y, *et al.*

Lab Invest 2015; 95: 469–479.

Summary: Epithelial mesenchymal transition (EMT) is the biological process in which epithelial cells change to a mesenchymal phenotype. EMT is vital during embryogenesis (type-I EMT), but can also be induced as a result of persistent tissue damage. There are then two subsequent possibilities: fibrosis (type-II EMT) and pre-malignant stroma when associated with angiogenesis (type-III EMT). In chronic obstructive pulmonary disease (COPD), EMT may contribute to small airway (SA) fibrosis (type-II EMT) and to cancer (type-III EMT).

In this study, the authors investigated the role of urokinase-type plasminogen activator (uPA) in inducing EMT in SAs of COPD patients. They seek evidence for EMT in lung tissue and epithelial cell lines. The data suggest that uPA is highly expressed in the SAs of smokers/COPD patients and is related to vimentin expression. Moreover, inhibition of uPA blocked EMT and reduced migration of cells. The authors suggest that uPA may contribute to SA fibrosis through EMT. However, the authors did not compare large airways (LAs), which are the major site for epithelial malignancies in COPD, with SAs for EMT and uPA expression. This warrants further studies, since uPA may be driving type-II EMT in SAs, contributing to fibrosis at this site, whereas type-III in LAs might be contributing to epithelial malignancies.

This study confirms the importance of EMT in smokers and in COPD and the contribution of uPA in driving EMT-related changes. It also suggests uPA as a potential therapeutic target. Understanding the role of EMT in COPD will lead to better understanding of pathogenesis of COPD and its relation to fibrosis and cancer and may have therapeutic implications.

Reviewed by: Sukhwinder Singh Sohal (Australia, Assembly 3)

Hot topic articles are short (approx. 200 words) summaries of recent important articles in respiratory medicine written by Junior ERS members (aged 35 years and under). To become a hot topic author please contact Neil Saad: e-mail: neil.saad11@imperial.ac.uk