Hot topics from the Assemblies

Cite as: Hot topics from the Assemblies. *Breathe* 2017; 13: 141–142.

Association of borderline pulmonary hypertension with mortality and hospitalization in a large patient cohort: insights from the Veterans Affairs Clinical Assessment, Reporting, and Tracking program

Authors: Maron BA, Hess E, Maddox TM, *et al.*
Circulation 2016; 133: 1240–1248.

Summary: Pulmonary hypertension (PH) diagnostic criteria are currently defined as a mean pulmonary arterial pressure (mPAP) ≥25 mmHg measured during a resting right heart catheterisation (RHC). However, the upper limit of normal for mPAP is believed to be around 20 mmHg. Patients with mPAP >20 mmHg but <25 mmHg are considered as having "borderline" PH. The clinical and prognostic relevance of this population is not completely understood.

In this study, using the Veterans Affairs Clinical Assessment, Reporting, and Tracking programme, Maron *et al.* aimed to assess the clinical relevance of borderline PH among 21 727 patients undergoing RHC.

The authors demonstrated that mortality risk increases with increasing resting mPAP, beginning at 19 mmHg, and that mPAP 19–24 mmHg is associated with a higher chance of hospitalisation and/or mortality compared to patients with mPAP <19 mmHg. The deleterious impact of borderline PH on patient's outcomes was maintained even after the exclusion of subjects with elevated resting pulmonary arterial wedge pressure and pulmonary vascular resistance.

This study is the largest to date to evaluate the association between increasing levels of resting mPAP currently considered to be normal, and rates of hospitalisation and mortality. The findings provide important additional framework for the understanding of the continuum of PH and suggest that borderline PH is clinically relevant to patients' outcomes. Further studies in independent populations are now needed.

Reviewed by: Rudolf K.F. Oliveira (Brazil, Assembly 4)

Blood eosinophils and outcomes in severe hospitalized exacerbations of COPD

Authors: Bafadhel M, Greening N, Harvey-Dunstan T, *et al.*
Chest 2016; 150: 320–328

Summary: The current treatment of chronic obstructive pulmonary disease (COPD) exacerbations includes systemic steroids, antibiotics or both. There is evidence that patients with eosinophilic, moderate-severity exacerbations (eosinophil cell count >2% of white blood cells) have better steroid response.

This study recruited subjects from a randomised clinical trial of an exercise-based recovery intervention. 243 patients with a smoking history of >10 pack-years with the diagnosis of COPD were enrolled. All patients had full blood counts on admission. Peripheral eosinophilia was observed in 25% of subjects (n=62, peripheral blood count >200 cells per µL or >2% of leukocytes). Patients with eosinophilia had a significantly lower C-reactive protein (CRP) (median (interquartile range) 13 (5–48) *versus* 55 (18–139) mg·dL^{-1}, p<0.001) and significantly shorter hospital stay compared to neutrophilic patients after corticosteroid treatment (mean (range) 5.0 (1–19) *versus* 6.5 (1–33) days, p<0.015). 69 patients had evidence of consolidation on chest radiography. After exclusion of these patients, CRP was still significantly lower in patients with eosinophilia. Pre-admission corticosteroid treatment had no significant effect on hospital stay.

In conclusion, eosinophilia can be identified in 25% of patients with COPD exacerbations. These patients have a higher risk of harm without systemic steroid treatment. As this study was a *post hoc* analysis, further studies are needed to corroborate the results.

Reviewed by: Peter Horvath (Hungary, Assembly 5)

Lung cancer subtypes generate unique immune responses

Authors: Busch SE, Hanke ML, Kargl J, *et al.*
J Immunol 2016; 197: 4493–4503

Summary: With regard to the recent developments in immune-checkpoint inhibitors for lung cancer therapy, Busch *et al.* investigated the relationship of the host's immune response to lung cancer with different mutational backgrounds and histological subtypes. They used three different mouse models of non-small cell lung cancer (NSCLC) adenocarcinoma (*Kras*$^{LSL\text{-}G12D}$, *Trp53*$^{Fl/Fl}$ and *Egfr*^{L858R}) as well as two (*Rb1*$^{Fl/Fl}$ and *Trp53*$^{Fl/Fl}$) for small cell lung cancer (SCLC). The models were based either on the insertion of a clinically relevant point mutation (*Kras*$^{LSL\text{-}G12D}$ and *Egfr*^{L858R}) or knock-out of the tumor-suppressor genes *Trp53* or *Rb1*. Overall, the immune response, as measured by the leukocyte (CD45^{+} cell) content in the tumor, was lower in SCLC compared to NSCLC in both animal models and human tissues. Most notably for adenocarcinomas, the *Egfr*-mutant

background resulted in a diminished T-cell response, as indicated by a reduced $CD3^+$ cell count within the tumors, fewer regulatory T-cells and $CD4^+$ T-helper cells, and no expansion of $CD8^+$ T-cells compared to *Kras*- and *Trp53*-driven models. Interestingly, the expression of PD-L1 (programmed death ligand 1), a therapy-relevant immune checkpoint molecule, on the tumor cells remained unaltered between the different mutational models while *Kras* seemed to blunt the natural killer cell function, as indicated by reduced cell number and reduced expression of the NKG2D receptor. The study elucidated the host's immune response to different types of lung cancer and the aggressiveness of SCLC might be reflected by the reduced immunogenicity. With regard to adenocarcinomas, the study adds important details regarding how certain mutations may differentially shape the local immune response.

Reviewed by: Sebastian Marwitz (Germany, Assembly 3)

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

The PEARL score predicts 90-day readmission or death after hospitalisation for acute exacerbation of COPD

Authors: Echevarria C, Steer J, Heslop-Marshall K, *et al.*

Thorax 2017 [in press https://doi.org/10.1136/thoraxjnl-2016-209298]

Summary: Echevarria *et al.* examined 2417 patients, of whom 936 (38.7%) were readmitted to hospital or died within 90 days of discharge. They identified five independent predictors of need for readmission or death within 90 days. This led to development of the PEARL prognostic score comprising five indices: previous admissions (severe exacerbation in the past year), extended Medical Research Council dyspnoea score, age, right-sided heart failure and left-sided heart failure. The authors showed that this score is a consistent and accurate predictor of 90-day readmission or death. Higher PEARL scores were associated with a shorter time to readmission. The area under receiver operator characteristic curve for 90-day readmission/death without readmission was shown to be 0.70, which is superior to other scores that have been used in this population such as ADO (age, dyspnoea and airflow obstruction), BODEX (body mass index, airflow obstruction, dyspnoea and exacerbations), DOSE (dyspnoea, obstruction, smoking and exacerbation) and LACE (length of stay, acuity of the admission, comorbidity and emergency department use).

The authors conclude that PEARL score is easy to apply at the bedside using indices that are routinely available in all patients and accurately risk stratifies patients according to risk of readmission. This score may be useful to inform post-discharge planning in patients admitted with acute exacerbation of COPD.

Reviewed by: Evgeni Mekov (Bulgaria, Assembly 1)