years in those without COPD. After adjusting for confounding by sex and stratifying for age, survival was shorter after 1st MI in patients with COPD; HR 1.57 (1.23 to 1.92, p<0.001) in those with COPD compared to those without COPD (Abstract S96 figure 1). Survival was shorter in those (n=96) who exacerbated within 6 months of their 1st MI; HR 1.72 (1.13 to 2.60, p=0.01).

Conclusions Survival is shorter after an “unanticipated” MI in patients with COPD and patients who exacerbate within 6 months of their MI have an even higher mortality rate.

BMPR-II mutations do not predispose to pulmonary arterial hypertension in a mouse model of schistosomiasis

A Crosby, E Soon, F Jones, M Southwood, B Dunmore, D Dunne, N W Morrell. Cambridge University, Cambridge, UK

Schistosomiasis is the worldwide leading cause of pulmonary arterial hypertension (PAH) and is particularly prevalent in the third-world. More than 80% of patients with PAH in the western world have a mutation in bone morphogenetic protein type-II receptor (BMPR-II), which is a member of the transforming growth receptor-β (TGF-β) superfamily and is important in cell proliferation and differentiation. The aim of the study was to determine if mice with a heterozygous null mutation in BMPR-II are more susceptible to schistosomiasis-induced PAH, compared to wild-type littersates.

Methods Wild-type and mutant C57/B16 mice were infected percutaneously with a low dose of S mansoni. At 17 weeks post-infection right ventricular systolic pressure (RVSP) and right ventricular (RV) hypertrophy, liver and lung egg counts and body weight were measured. Pulmonary vascular remodelling was assessed by morphometry, following immunohistochemistry. Human and mouse pulmonary arterial smooth muscle cells (PASMC) were cultured with S mansoni eggs for 24 h. At 24 h the expression of cytokines in PASMC were measured by qPCR and cytokine levels in the cell supernatant were measured by ELISA.

Results There was a significant increase in RVSP, the degree of RV hypertrophy, liver weight or body weight between wild-type or mutant mice. However, 35% of the mutant mice died prematurely. After 24 h culture with eggs both mouse and human PASMC showed an increase in cytokine expression and cytokine release. More specifically we saw an increase in IL-6, Kc (mouse homologue of IL-8) and IL-1β expression and an increase in IL-6 and Kc secretion. We also saw an increase in PASMC proliferation, determined by Ki67. There was a suggestion that PASMC from mutant mice may display an increase in cytokine response to egg stimulation.

Conclusions This study has shown that BMPR-II mutations do not predispose to schistosomiasis-induced PAH. We have also shown that PASMC respond to S mansoni eggs by an increase in expression and release of inflammatory cytokines. These may play a part in inducing pulmonary vascular remodelling by stimulating PASMC proliferation. However, this effect was not significantly enhanced by BMPR-II mutations.

The anti-malarial drug and lysosomal inhibitor, chloroquine, increases cell surface expression of BMPR-II


Bone morphogenetic protein receptor type II (BMPR-II) is a member of the transforming growth factor β (TGFβ) receptor superfamily.