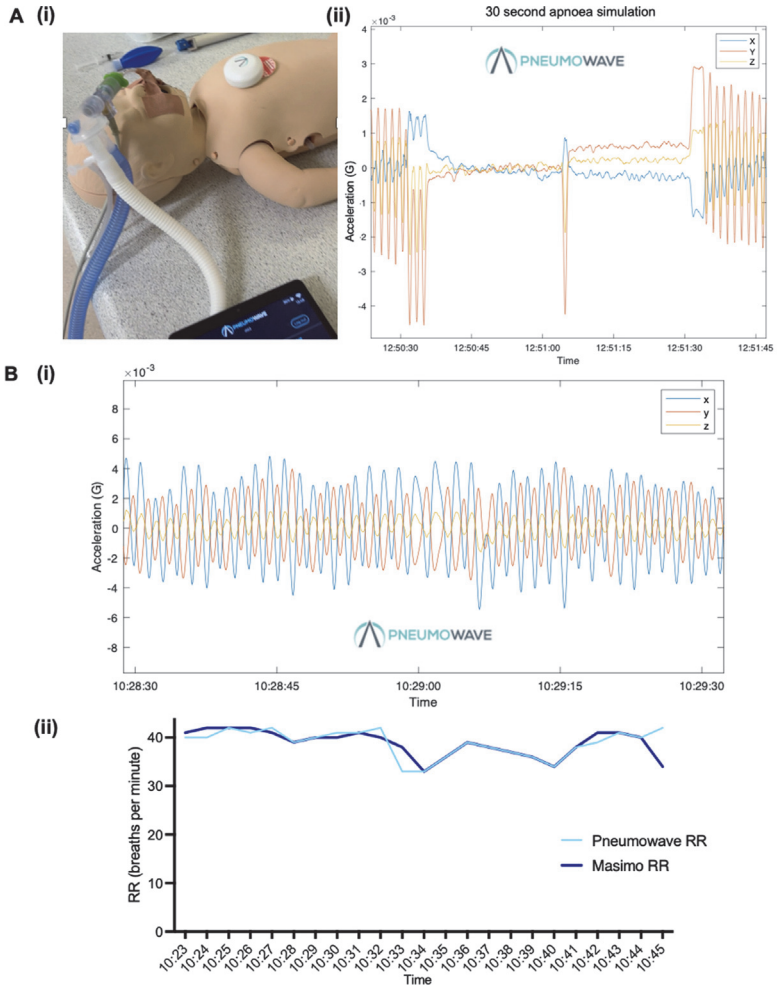

Abstract P106 Figure 1 (A) Pre-clinical work with ventilator and neonatal mannequin, (i) mannequin and ventilator set up (ii) 30 second periods of apnoea shown on accelerometer data (x, y and z axis) (B) Pneumowave accelerometer data compared with standard clinical monitoring data. 3-week-old neonate, born 38+6/40, weighing 3850g on 0.2L/min supplemental O_2. (i) Pneumowave data (x, y and z axis) collected from chest worn biosensor (ii) Pneumowave Respiration rate (RR) compared with Masimo Rad 97 RRp, respiration rate based on plethysmographic waveform

'The Man in the Iron Mask' – Acute respiratory support

P107 VASCULAR ENDOTHELIAL GROWTH FACTOR AND ACUTE RESPIRATORY DISTRESS SYNDROME: A MENDELIAN RANDOMISATION STUDY

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Introduction Acute respiratory distress syndrome (ARDS) is a severe inflammatory lung disorder mainly caused by sepsis resulting from both pulmonary and non-pulmonary infections. ARDS is characterised by rapid onset of acute respiratory failure and has a hospital mortality of about 40%. A previous genome-wide association study (GWAS) of sepsis-associated ARDS revealed an association between genes in the vascular endothelial growth factor signalling pathway (*VEGFA* and *VEGFR1*) and ARDS susceptibility.[1]

Objective Assess the causal relationship between VEGFA and VEGFR1 circulating levels and ARDS risk.

Methods We used two-sample bidirectional Mendelian randomisation (MR) to test the causal effect of VEGFA and VEGFR1 serum levels on ARDS, and of ARDS on VEGFA and

VEGFR1 serum levels. We used genetic variants from GWAS of both VEGFA and VEGFR1 serum levels (UK Biobank, N=46,836) and of sepsis-associated ARDS (N= 274 ARDS cases and 316 controls with sepsis) as instrumental variables. We used the inverse variance-weighted (IVW) method to test causality and performed sensitivity analyses with five additional methods. We evaluated presence of pleiotropy and outliers. MR-RAPS was used to test weak instrumental variables ($p<0.05$).

Results No significant causal effect on ARDS risk was observed for either VEGFA (pIVW=0.992) or VEGFR1 (pIVW=0.924) serum levels based on our findings. Similarly, we found no indication that ARDS has a causal effect on either VEGFA (pIVW=0.487) or VEGFR1 (pIVW=0.168) serum levels. Sensitivity analyses supported these results.

Conclusions Our results do not provide evidence for a causal link between serum levels of VEGFA or VEGFR1 and susceptibility to sepsis-associated ARDS. Further analyses are required to explore the impact of VEGF regulation during the acute phase on the development of ARDS.

REFERENCE

1. Guillen-Guio, *et al. Lancet Respir Med.* 2020;**8**:258–266. PMC7772505.

P108 THE ROLE OF PROPROTEIN CONVERTASE SUBTILISIN-KEXIN TYPE 9 IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

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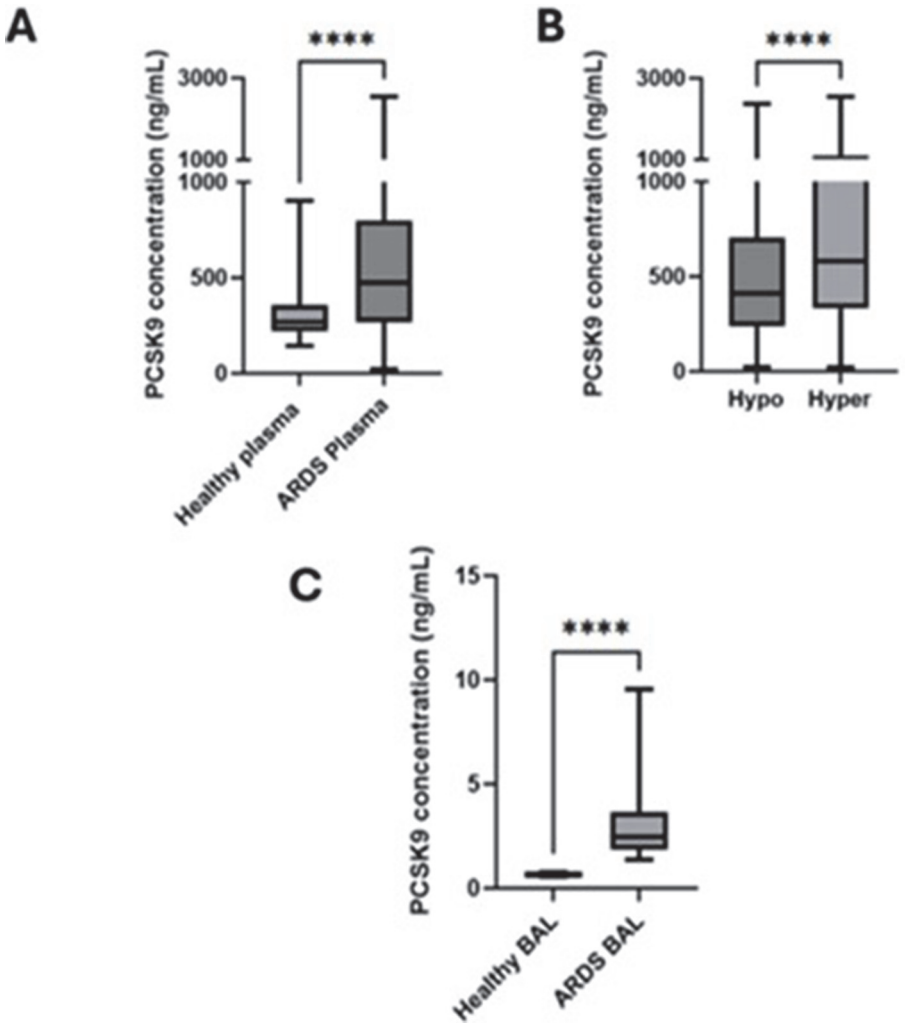
Background Proprotein Convertase Subtilisin-Kexin type 9 (PCSK9) is a key regulator of lipid metabolism. Recently, a pro-inflammatory role for PCSK9 has been hypothesised, through reduced bacterial phospholipid clearance. Elevated circulating PCSK9 levels in patients with acute respiratory distress syndrome (ARDS) has been reported in a single cohort, leading to the hypothesis that PCSK9 plays a role in ARDS pathogenesis.

This study aimed to replicate the finding that circulating PCSK9 levels are elevated in ARDS, investigate the association between PCSK9 and clinical outcomes, and explore whether PCSK9 levels are increased in the alveolar compartment (in bronchoalveolar lavage (BAL) fluid). A further aim was to compare circulating PCSK9 levels between patients with the



Abstract P108 Figure 1 PCSK9 concentration (ng/mL) determined by ELISA in A) Plasma from ARDS patients compared to healthy volunteers (p<0.0001). B) Plasma from ARDS patients in hyperinflammatory compared to hypoinflammatory subphenotypes/(p<0.0001). C) BAL fluid from ARDS patients compared to healthy volunteers (p<0.0001)