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TITLE: Hemodynamic Effect of Bronchodilation in a Porcine Model of Acute Pulmonary Embolism

BACKGROUND: Increased pulmonary vascular resistance (PVR) is the primary driver of mortality in pulmonary embolism (PE). Vasoactive compounds and neurogenic reflexes also induce bronchoconstriction, contributing to hypoxemia and further exacerbating pulmonary vasoconstriction via autoregulation in the pulmonary vasculature. Bronchodilators such as short-acting beta2-adrenergic agonists may reduce PVR in PE given this interplay, but this has not been investigated.

METHODS: In this randomized, controlled, assessor-blinded study, acute PE was induced with autologous clots in 14 female Landrace pigs. Animals were randomized to inhaled salbutamol (n=7) or saline (n=7), delivered by mesh nebulization in the ventilator circuit as three escalating doses at 30-minute intervals (IH1: 1 mg, IH2: 3 mg, IH3: 10 mg). Finally, a 100% oxygen challenge was performed to assess the residual hypoxic vasoconstrictive component. Hemodynamics were assessed by invasive pressures and right heart catheterization after each inhalation and oxygen challenge.

RESULTS: Post-PE PVR was higher in the salbutamol group (345 vs. 246 dyn·s·cm⁻⁵); all estimates are adjusted for post-PE values. Salbutamol lowered PVR dose-dependently (p for trend=0.021), to a ratio of 0.49 (0.36–0.67; p<0.001) at IH3. This was driven by increased cardiac output (2.06 [1.63–2.59]; p<0.001) with unchanged mean pulmonary arterial pressure (1.02 [0.86–1.21]; p=0.81). Heart rate was unaffected at IH1 (1.05 [0.93–1.19]) but rose to 1.65 (1.45–1.87; p<0.001) at IH3. The PVR/systemic vascular resistance ratio was 0.85 (0.69–1.04) at IH1 and 1.02 (0.83–1.25) at IH3 (p for trend=0.012).

CONCLUSION: Inhaled salbutamol reduced PVR dose-dependently in experimental acute PE, driven by increased cardiac output rather than reduced pulmonary arterial pressure. Suggested pulmonary selectivity was present only at the lowest dose and was lost as systemic beta-adrenergic effects emerged. Further studies should investigate whether low-dose salbutamol offers pulmonary-selective benefit in PE.

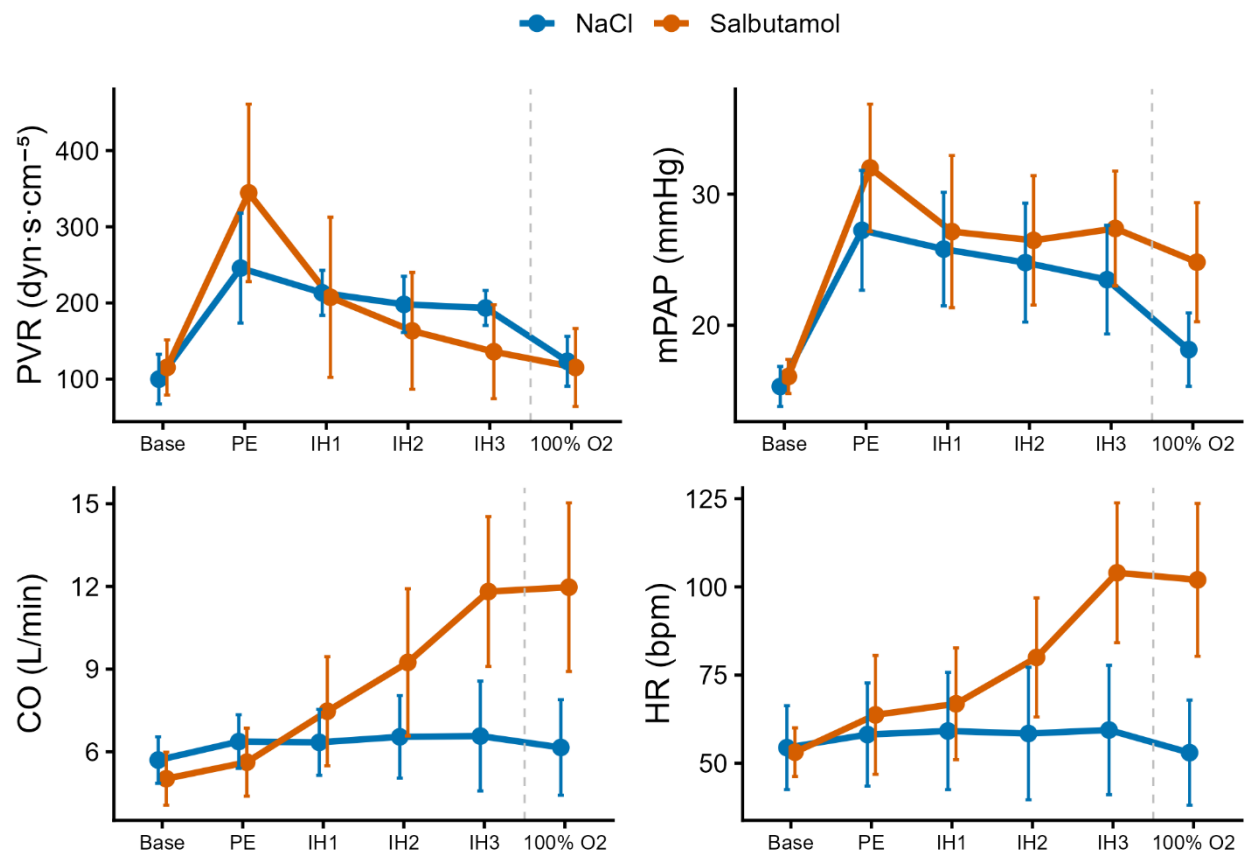


Figure 1. Hemodynamics during escalating doses of inhaled salbutamol (n = 7) or saline (n = 7) in acute pulmonary embolism, with a final 100 % oxygen challenge. Mean $\pm$ SD of observed unadjusted values. PVR, pulmonary vascular resistance; mPAP, mean pulmonary arterial pressure; CO, cardiac output; HR, heart rate.