題名:Nitric oxide modulates air embolism-induced lung injury in rats with normotension and hypertension

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摘要:1. Air embolism the in lungs induces microvascular obstruction, mediator release and acute lung injury (ALI). Nitrite oxide (NO) plays protective and pathological roles in ALI produced by various causes, but its role in air embolism-induced ALI has not been fully investigated. 2. The purpose of the present investigation was to elucidate the involvement of NO and pro-inflammatory cytokines in the pathogenesis of ALI following air infusion into isolated perfused lungs from spontaneously hypertensive rats (SHR) and normotensive Wistar Kyoto (WKY) rats. 3. The extent of ALI was evaluated by changes in lung weight, Evans blue dye leakage, the protein concentration in the bronchoalveolar lavage and pathological examination. We also measured nitrite/nitrate (NO(x)), tumour necrosis factor (TNF)-alpha and interleukin (IL)-1beta concentrations in lung perfusate and determined cGMP in lung tissue. 4. The NO synthase (NOS) inhibitors N(G)-nitro-l-arginine methyl ester (l-NAME) and l-N(6)-(1-iminoethyl)-lysine (l-Nil), as well as the NO donors sodium nitroprusside (SNP) and s-nitroso-N-acetylpenicillamine (SNAP), were administered 30 min before air embolism at a concentration of 10(-3) mol/L in the lung perfusate. 5. Air embolism-induced ALI was enhanced by pretreatment with l-NAME or l-Nil, but was alleviated by SNP or SNAP pretreatment, in both SHR and WKY rats. In both SHR and WKY rats, AE elevated levels of NO(x) (2.6 and 28.7%, respectively), TNF-alpha (52.7 and 158.6%, respectively) and IL-1beta (108.4 and 224.1%, respectively) in the lung perfusate and cGMP

levels in lung tissues (35.8 and 111.2%, respectively). Pretreatment with l-LAME or l-Nil exacerbated, whereas SNP or SNAP abrogated, the increases in these factors, except in the case of NO(x) (levels were decreased by l-LAME or l-Nil pretreatment and increased by SNP or SNAP pretreatment). 6. Air embolism caused increases in the lung weight (LW)/bodyweight ratio, LW gain, protein concentration in bronchoalveolar lavage and Evans blue dye leakage. These AE-induced changes were less in lungs isolated from SHR compared with normotensive WKY rats. 7. The results suggest that ALI and associated changes following air embolism in lungs isolated from SHR are less than those in WKY rats. Nitric oxide production through inducible NOS isoforms reduces air embolism-induced lung injury and associated changes. Spontaneously hypertensive rats appear to be more resistant than WKY rats to air embolism challenge.