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Title: Changes in airway and lung tissue mechanics in aspiration-induced lung injury: Differentiation of direct and indirect mechanisms in a porcine model

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Body: Aspiration of gastric content deteriorates lung function directly by epithelial cell damage and/or by indirect effects related to neurohumoral pathways. To distinguish these distinct effects, the two main bronchi were selectively intubated in anaesthetized, thoracotomized, mechanically ventilated pigs while PEEP of 4 (n=7) or 10 cmH₂O (n=6) was maintained. The right lung was then provoked by instilling 0.5 ml/kg gastric juice (pH=2), while the left lung remained unaffected. Pulmonary input impedance (ZL) was measured separately in both lungs before aspiration and for 120 min thereafter. Airway resistance (Raw), tissue damping (G) and elastance (H) were derived from the ZL spectra for both lungs by model fitting. Marked transient elevations in Raw, G and H were observed in the affected lung with peak increases occurring at 5-15 min. These increases were greater with PEEP 4 than PEEP 10 in the challenged right lung (Raw: 213±130[SE]% vs. 61±39%, G: 638±362% vs. 267±259%, H: 302±188% vs. 49±50%; p<0.05), whereas no increases were detected in the intact left lung. These findings evidence that the magnitude and the duration of the lung damage following aspiration of gastric content are more moderate with PEEP 10 than PEEP 4. The lack of detrimental change in the intact lung indicates that the indirect neurohumorally-mediated bronchoconstriction plays a less significant role in the lung function deterioration after gastric content aspiration, which may result from the opposing effects of elevated vagal tone and the endogenous release of catecholamines with relaxation potentials. Grant support: OTKA K81179, TAMOP 4.2.2.A-11/1/KONV-2012-0052.