Summary

The main objective of our prospective experimental study was to develop a clinically relevant model of mechanical ventilation of healthy and damaged lungs ventilated for 12 hours. A widely recommended Vt=6ml/kg was used in comparison with commonly used Vt=10ml/kg. The study included a total of 52 piglets of domestic pig (Sus scrofa f. domestica) age 5-9 weeks. Piglets were divided into 3 groups: group B - Vt = 6ml/kg (11 piglets, 8 died), group C - Vt = 10ml/kg (21 piglets, 5 died) and group D - Vt= 50 ml + instillation of 50 ml saline into the trachea (6 piglets, 1 died).

In the presented study we focused on the influence of mechanical ventilation on several organ systems as well as induction of systemic inflammatory reaction. By using higher tidal volume, we aimed to induce possible biotraumatic changes. The ventilator settings were deliberately not changed during the study, except the change of Fi02 values based on the Sp02 value.

The first goal was to assess the influence of two different strategies of mechanical ventilation and induced lung injury on respiratory functions of the lungs and pulmonary mechanics. Piglets ventilated with Vt = 6ml/kg maintain the physiological oxemia, but the level of capnia increased over time with an adequate effect on acid-base balance. The highest mortality in this group is partially explained by a relative reduction of minute ventilation and respiratory acidosis induction. No changes of ventilatory indexes (AaDO2, RI, PaO2/FiO2) were observed, the function of alveolocapilarry membrane and oxygen diffusion were preserved. Group C was characterised by maintenance of obligatory ventilatory parameters (oxemia and capnia) in the physiologic range. Deterioration of indexes of ventilation during the experiment (AaDO2, OI, PaO2/FiO2) documented disturbance of gases diffusion across the alveolar- capilarry membrane. The decrease of dynamic compliance was simultaneously observed. Physiological values of oxemia and indexes of ventilation clearly declined during the experiment in animals exposed to non protective ventilation and lung injury (group D). Protective setting of tidal volume temporarily guarantees optimal quality of lung mechanics and does not guarantee optimal elimination of CO2. Non protective setting of tidal volume negatively affects lung mechanics and results to impairment of oxygen diffusion. The combination of lung injury and non protective ventilation further potentiates these negative changes.

The second objective was to evaluate the effect of mechanical ventilation on the function of extrapulmonary organs and systems, liver and kidney function. The signs of the renin-

angiotensin-aldosterone system activation as well as one-hour diuresis decrease and increase of urinary osmolality were observed in all groups. The activation of aldosterone was documented with reversed ratio of ions in the urine. The decrease in diuresis was significant especially in the non protective ventilated animals with lung injury. The increase of urea and creatinine occurred simultaneously in this group.

The third objective was to evaluate the effect of mechanical ventilation on the circulation and the possible development of systemic inflammatory response. No changes of invasively measured blood pressure and no changes in cardiac functions /assessed by transthoracal echocardiography/ were observed during the study.
The development of systemic inflammatory response was assessed by measuring levels of proinflammatory cytokines and adhesion molecules. There was an increase of IL-6 in all groups, the most significant elevation was observed in animals exposed to non protective ventilation and lung injury.
The levels of TNF-a suprisingly decreased in all groups during the study. The levels of intercellular and vascular adhesion molecules (p-ICAM a p-VCAM) did not change throughout the 12 hours of mechanical ventilation.

The fourth goal of our study was the evaluation of morphological changes of lungs and extrapulmonary organs. The macroscopical changes documented signs of hyperinflation alternating with signs of vascular congestion in the lung tissue exposed to ventilation with higher tidal volumes. These changes were located mainly in the dependent areas of lungs. The lung tissue exposed to protective ventilation did not demonstrate any major macroscopical pathological changes. The histological examination (light microscopy) of the lung tissue exposed to non protective ventilation documented inflammatory infiltration in the alveolar septa, bronchioles and vascular structures. The histological analysis of the lung tissue exposed to protective ventilation demonstrated mild inflammatory infiltration of alveolar septa. The microscopical examination of left ventricular myocardium, liver, kidney of both groups did not reveal any pathological changes.

In conclusion, the transition from spontaneous breathing to invasive mechanical ventilation affects the physiological processes of the organism. Protective mechanical ventilation does not guarantee a preservation of physiological processes in the lung tissue, but guarantees an

unchanged function and morphology of the extrapulmonary organs and systems. Mechanical ventilation with Vt = 10ml/kg does not fulfill the criteria for protective ventilation.