Supplemental Digital Content 3

Gas Exchange, Lung Volume, and Wet/Dry Ratio in Controls

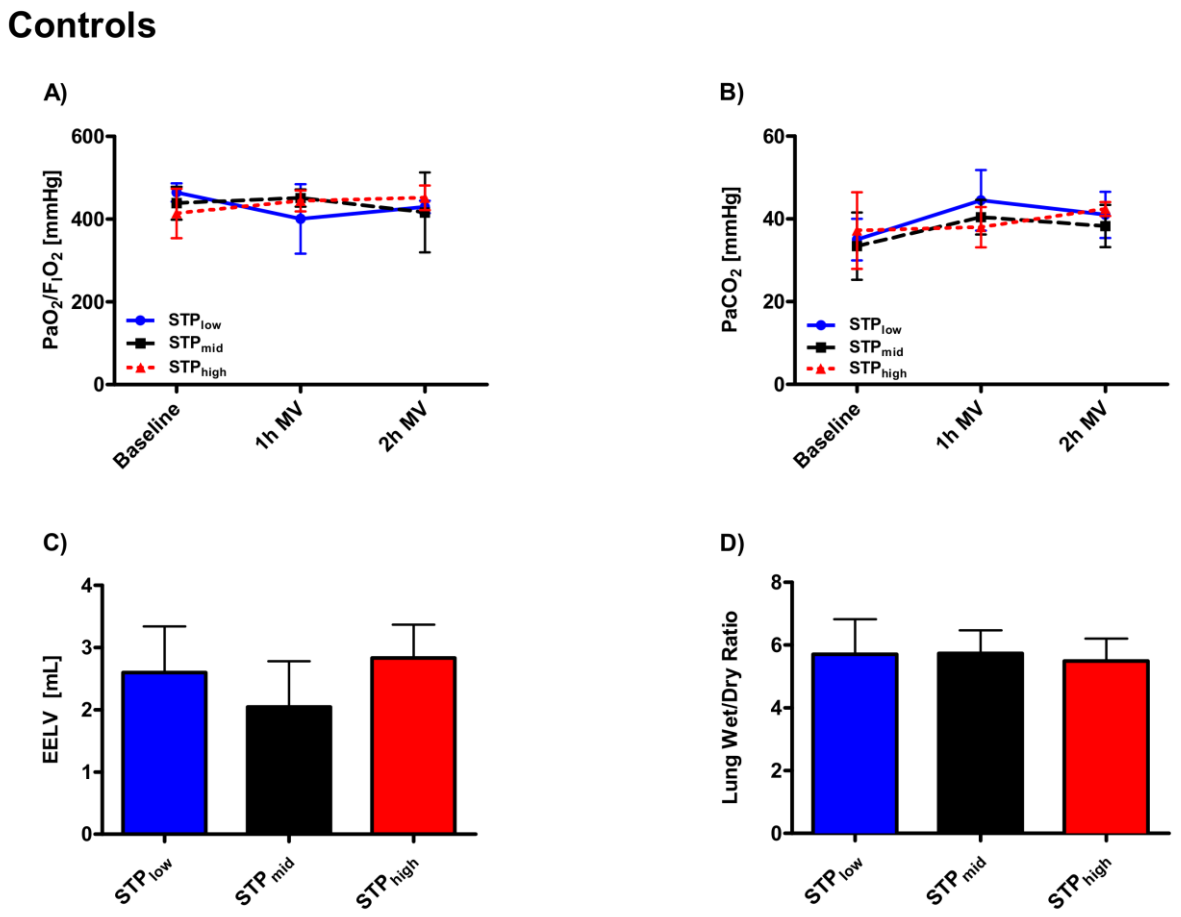


Fig. 1. Data are given as mean ± SD. Comparisons among groups were performed using two-way ANOVA. (A) fraction of arterial partial pressure of oxygen and inspired oxygen fraction (PaO_2/FIO_2); (B) arterial partial pressure of carbon dioxide ($PaCO_2$) and one-way ANOVA; (C) end-expiratory lung volume (EELV); (D) lung wet/dry ratio).

I:E = inspiratory-to-expiratory; MV = mechanical ventilation; STP_{high} = high levels of stress *vs.* time product (I:E 2:1); STP_{low} = low level of stress *vs.* time product (I:E 1:2); STP_{mid} = middle level of stress *vs.* time product (I:E 1:1).

Hemodynamics in Controls

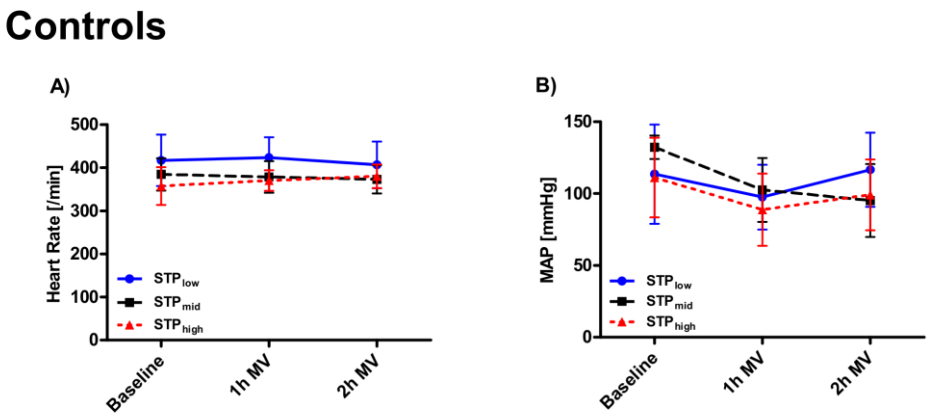


Fig. 2. Data are given as mean ± SD. Comparisons among groups were performed using two-way ANOVA. (A) heart rate; (B) mean arterial pressure (MAP).

I:E = inspiratory-to-expiratory; MV = mechanical ventilation; STP_{high} = high levels of stress *vs.* time product (I:E 2:1); STP_{low} = low level of stress *vs.* time product (I:E 1:2); STP_{mid} = middle level of stress *vs.* time product (I:E 1:1).

Respiratory Mechanics in Controls

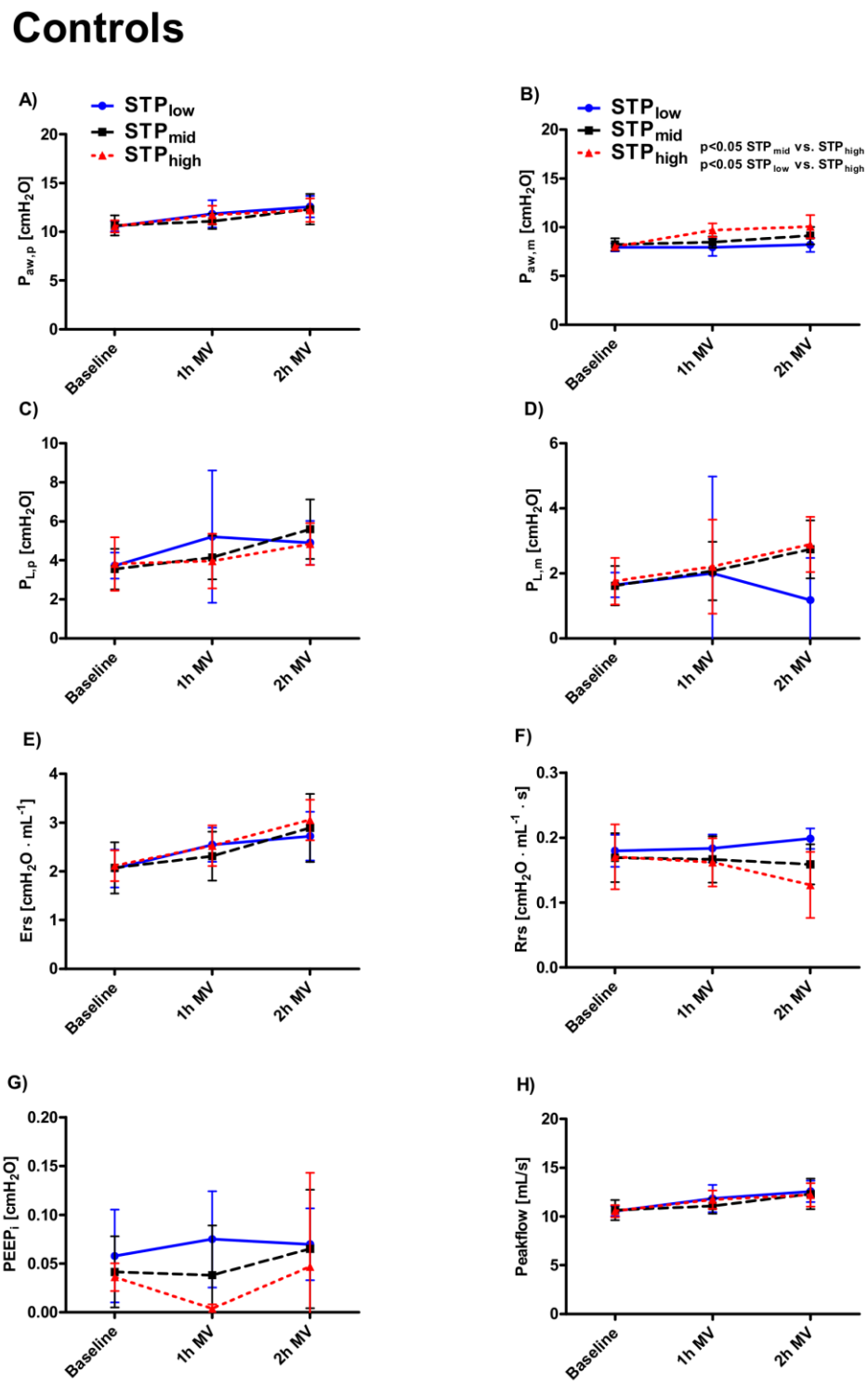


Fig. 3. Data are given as mean ± SD. Comparisons among groups were performed using two-way ANOVA. (A) $P_{aw,p}$ (peak airway pressure); (B) $P_{aw,m}$ (mean airway pressure); (C) $P_{L,p}$ (peak transpulmonary pressure); (D) $P_{L,m}$ (mean transpulmonary pressure); (E) E_{rs} (elastance

of the respiratory system); (F) R_{rs} (resistance of the respiratory system); (G) $PEEP_i$ (dynamic intrinsic positive end-expiratory pressure); (H) peak flow.

I:E = inspiratory-to-expiratory; MV= mechanical ventilation; STP_{high} = high levels of stress *vs.* time product (I:E 2:1); STP_{low} = low level of stress *vs.* time product (I:E 1:2); STP_{mid} = middle level of stress *vs.* time product (I:E 1:1).

Gene Expression in Controls

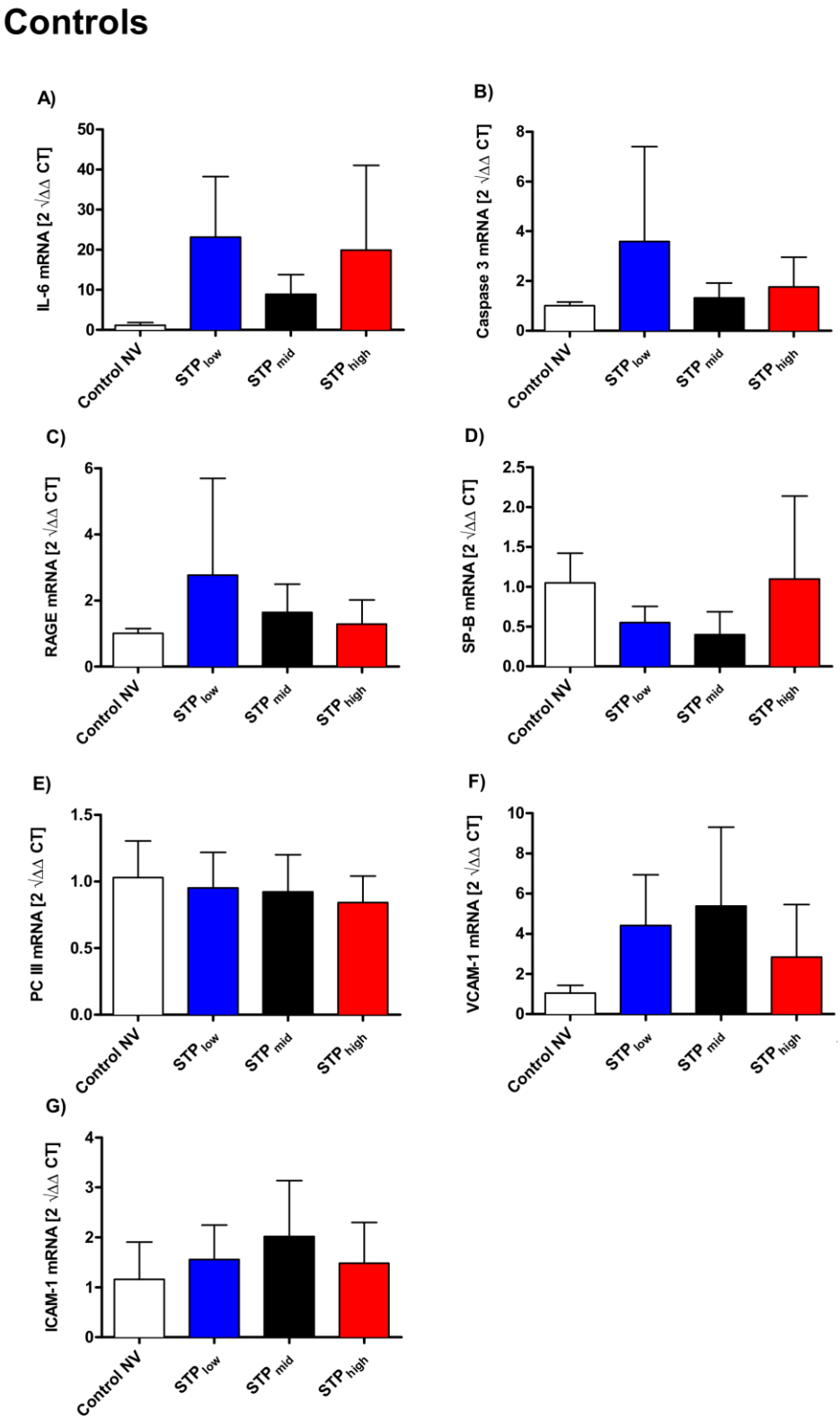
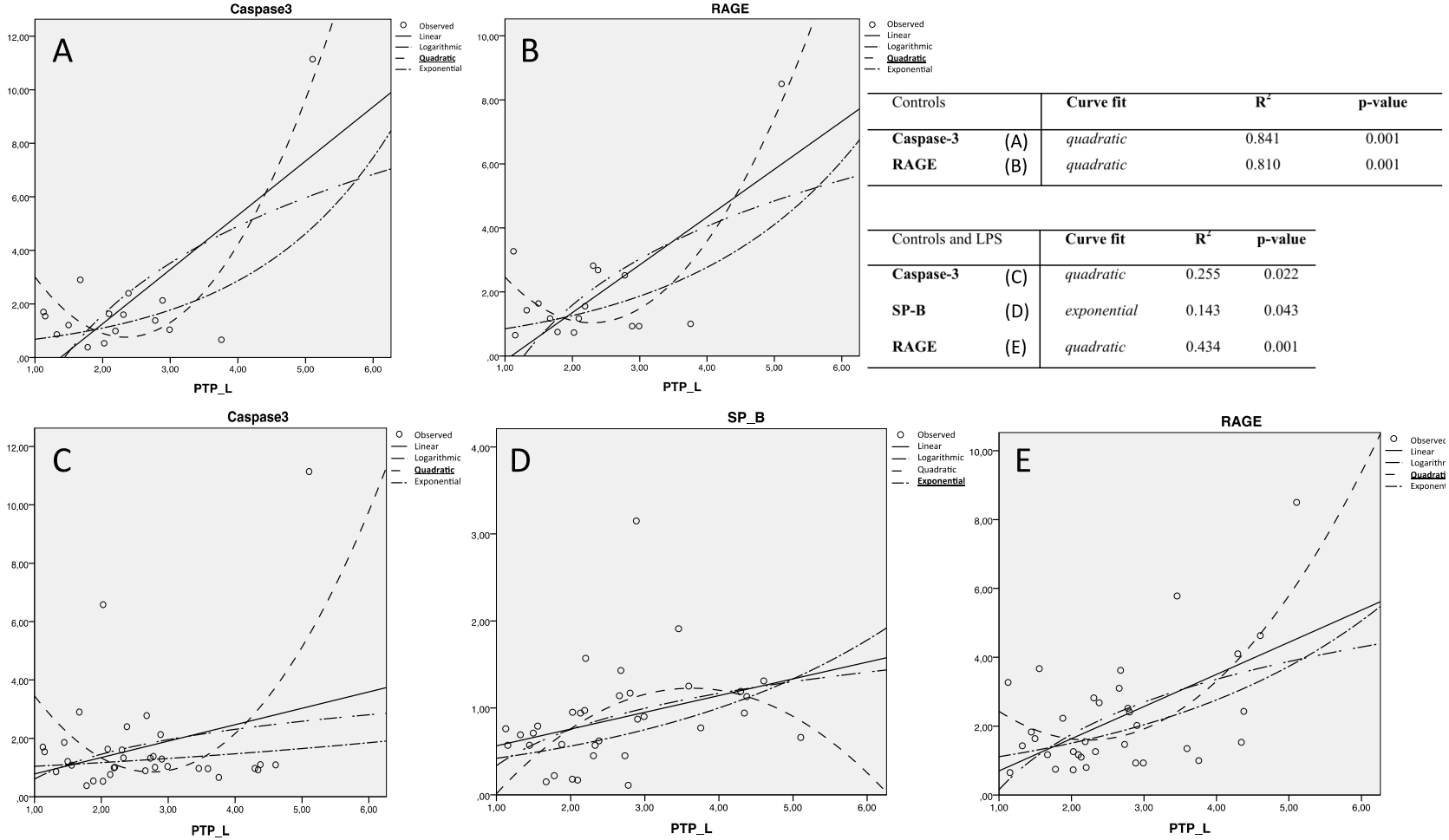


Fig. 4. Data are given as mean ± SD. Comparisons among groups were performed using one-way ANOVA. messenger RNA (mRNA) expressions of genes are normalized to the

respective housekeeping gene (glyceraldehyde 3-phosphate dehydrogenase). (A) IL-6 (interleukin-6); (B) caspase 3; (C) RAGE (receptor of advanced glycation end-products); (D) SP-B (surfactant protein B); (E) PC III (type III procollagen); (F) VCAM-1 (vascular cell adhesion molecule-1); (G) ICAM-1 = (intercellular cell adhesion molecule-1).

Control NV = nonventilated control animals; I:E = inspiratory-to-expiratory; MV = mechanical ventilation; STP_{high} = high levels of stress *vs.* time product (I:E 2:1); STP_{low} = low level of stress *vs.* time product (I:E 1:2); STP_{mid} = middle level of stress *vs.* time product (I:E 1:1).

Regression Analyses between Transpulmonary Pressure-time Product and Expression of Selected Genes in Lung Tissue



Controls		Curve fit	R^2	p-value
Caspase-3	(A)	*quadratic*	0.841	0.001
RAGE	(B)	*quadratic*	0.810	0.001

Controls and LPS		Curve fit	R^2	p-value
Caspase-3	(C)	*quadratic*	0.255	0.022
SP-B	(D)	*exponential*	0.143	0.043
RAGE	(E)	*quadratic*	0.434	0.001

Fig. 5. Results of the stepwise curve-fit regression analyses. Transpulmonary pressure time product (PTP_L, in $cmH_2O.s$) was used as nondependent variable while postmortem measurements of caspase 3, receptor for advanced glycation end products (RAGE) and surfactant protein-B (SP-B) were

used as dependent variables (ratio). Panels A and B show curve fit regression analysis in Control animals and panels C, D, and E, in Control combined with lipopolysaccharide-treated animals. Stepwise curve fits were calculated for linear, logarithmic, quadratic and exponential functions. Best model fits were determined by highest R^2 values.