## Conservative Versus Liberal Oxygenation Targets for Mechanically Ventilated Patients – a Pilot Multicenter Randomized Controlled Trial.

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Rationale: There are no randomized controlled trials (RCTs) comparing different oxygenation targets for Intensive Care Unit (ICU) patients.

**Objectives**: To determine whether a conservative oxygenation strategy is a feasible and acceptably safe alternative to a liberal oxygenation strategy among ICU patients requiring invasive mechanical ventilation (IMV).

**Methods**: At four multidisciplinary ICUs, 103 adult patients deemed likely to require IMV for  $\geq$ 24 hours were randomly allocated to either a conservative oxygenation strategy with a target SpO<sub>2</sub> of 88-92% (n=52) or a liberal oxygenation strategy with a target SpO<sub>2</sub> of  $\geq$ 96% (n=51).

Measurements and Main Results: The mean area-under-curve and 95% confidence interval (CI) for SpO<sub>2</sub> [93.4% (92.9-93.9%) versus 97% (96.5-97.5%)], SaO<sub>2</sub> [93.5% (93.1-94%) versus 96.8% (96.3-97.3%)], PaO<sub>2</sub> [70 (68-73) mmHg versus 92 (89-96) mmHg] and FiO<sub>2</sub> [0.26 (0.25-0.28) versus 0.36 (0.34-0.39)] in the conservative versus liberal oxygenation arm were significantly different (p<0.0001 for all). There were no significant between-group differences in any measures of organ dysfunction, or ICU or 90-day mortality. The percentage time spent with a SpO<sub>2</sub> <88% in the conservative versus liberal arm was 1% versus 0.3% (p=0.03), and percentage time spent with a SpO<sub>2</sub> >98% in conservative versus liberal arm was 4% versus 22% (p<0.001). The adjusted hazard ratio for 90-day mortality in the conservative arm was 0.77 (95%CI: 0.40-1.50; p=0.44) overall and 0.49 (95% CI: 0.20-1.17; p=0.10) in the pre-specified subgroup of patients with a baseline PaO<sub>2</sub>/FiO<sub>2</sub> <300.

**Conclusions**: Our study supports the feasibility and acceptable safety of a conservative oxygenation strategy in patients receiving invasive MV. Larger RCTs of this intervention appear justified.