

Automated Titration of Vasopressor Infusion Using a Novel Closed-Loop Controller: In Vivo Feasibility Study Using a Swine Model

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Background: Multiple large retrospective studies have reported associations between intraoperative hypotension and adverse postoperative complications. One of the most common interventions in the management of hypotension is vasopressor administration. Unfortunately, this approach requires careful and frequent vasopressor boluses and/or multiple adjustments of an infusion. We recently developed a closed-loop controller that titrates vasopressors to maintain mean arterial pressure (MAP) within set limits. Here we assessed the safety, feasibility and overall performance of this system in a swine model. We hypothesized that the closed-loop controller would be able to maintain MAP at a steady, predefined target level of 80 mmHg for more than 85% of the time.

Methods: We randomized 14 healthy anesthetized pigs (42 ± 6 kg) either to a control group or a closed-loop group (7 per group). Using infusions of sodium nitroprusside at doses between 65 and 130 $\mu\text{g}/\text{min}$ we induced four normovolemic hypotensive challenges of 30 minutes each. In the control group, nothing was done to correct hypotension. In the closed-loop group, the system automatically titrated norepinephrine doses to achieve a predetermined MAP of 80 mmHg. The primary objective was study time spent within ± 5 mmHg of the MAP target. Secondary objectives were the Varvel criteria (performance error (PE), median PE, median absolute PE, wobble and divergence).

Results: The closed-loop controller maintained MAP within ± 5 mmHg of the target for $98\pm 1\%$ (mean \pm SD) of the time. In the control group, the MAP was 80 ± 5 mmHg for $14.0 \pm 2.8\%$ of the time ($p < 0.0001$). The MAP in the closed-loop group was above the target range for $1.2\pm 1.2\%$ and below it for $0.5\pm 0.9\%$ of the time (**FIGURE 1**). The Varvel performance criteria were all optimal.

Conclusion: In this experimental model of induced normovolemic hypotensive episodes in healthy pigs, an automated closed-loop system accurately titrated norepinephrine infusion to correct hypotension.

MEAN ARTERIAL PRESSURE IN ALL ANIMALS

