Published in final edited form as:

J Trauma Acute Care Surg. 2015 July ; 79(1): 53–59. doi:10.1097/TA.0000000000000680.

Portable mechanical ventilation with closed-loop control of inspired fraction of oxygen maintains oxygenation in the setting of hemorrhage and lung injury

Peter L. Jernigan, MD, Richard S. Hoehn, MD, Thomas C. Blakeman, MSc, RRT, Judy Heyl, RVT, Bryce R.H. Robinson, MD, Timothy A. Pritts, MD, PhD, and Richard D. Branson, MSc, RRT

Division of Trauma and Critical Care, Department of Surgery, Institute for Military Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio

Abstract

BACKGROUND—Closed-loop controllers (CLCs) embedded within portable mechanical ventilators may allow for autonomous weaning. The ability of CLCs to maintain adequate oxygenation in the setting of hemorrhage and lung injury is unknown. We hypothesized that a portable ventilator with a CLC for inspired fraction of oxygen (FIO₂) could provide oxygenation in a porcine model of hemorrhage and lung injury.

METHODS—Female pigs randomized to the study group (n = 6) underwent a pressure-controlled bleed (mean arterial pressure = 40 mm Hg for 30 minutes). Acute lung injury was induced by saline lung lavage followed by intentional infliction of barotrauma. Sham pigs (n = 6) underwent placement of monitoring devices without hemorrhage or lung injury. All pigs were then placed on a portable ventilator modified with a CLC algorithm, which uses feedback from pulse oximetry (SpO₂) and FIO₂ trends to adjust FIO₂ and maintain a target SpO₂ of 94% (2%). The initial FIO₂ was set at 0.60. Tidal volume, positive end-expiratory pressure, rate, and inspiratory-to-expiratory ratio were constant unless changes were required clinically.

RESULTS—Study pigs had lower mean arterial pressures than shams at all time points except baseline. PaO₂/FIO₂ ratios were less than 300 and significantly lower than both baseline values and corresponding sham values at all time points. The CLC weaned the FIO₂ at a reduced rate in study pigs relative to shams with a final mean FIO₂ of 0.54 and 0.29 in study and sham pigs,

Address for reprints: Bryce R. Robinson, MD, Division of Trauma and Critical Care, Department of Surgery, Institute for Military Medicine, University of Cincinnati College of Medicine, 231 Albert Sabin Way, Cincinnati, OH 45267-0558; bryce.robinson@uc.edu.

This study was presented at the 28th Annual Scientific Assembly of the Eastern Association for the Surgery of Trauma, January 13–17, 2015, in Lake Buena Vista, Florida.

AUTHORSHIP

P.L.J. contributed to all portions of the study as follows: literature search, study design, data collection, data analysis, data interpretation, manuscript writing, and critical revision. R.S.H. and T.C.B. contributed to the literature review, study design, data collection, data analysis, data interpretation, manuscript writing, and critical revision. J.H. contributed to the study design, data collection, data analysis, and animal care. B.R.R. contributed to the literature search, study design, data analysis, data interpretation, manuscript writing, and critical revision. T.A.P. contributed to the literature search, study design, data interpretation, manuscript writing, and critical revision. R.D.B. contributed to all portions of the study as follows: literature search, study design, data collection, data analysis, data interpretation, manuscript revision, and critical revision.

DISCLOSURE

None of the other authors have any disclosures to report.

respectively ($p < 0.05$). There was a significant divergence in the study and sham FIO₂ curves but no significant difference in oxygen saturation or hypoxemia.

CONCLUSION—Adequate oxygenation can be maintained in the setting of hemorrhage and lung injury using a portable ventilator embedded with a CLC of FIO₂ based on pulse oximetry. These devices may be valuable for providing advanced medical care in resource-limited environments.

Keywords

Closed-loop ventilation; oxygenation; lung injury; hemorrhagic shock; pigs

Achieving and maintaining an appropriate level of oxygenation is one of the primary goals of mechanical ventilation. Oxygen saturation in the blood can be determined by noninvasive pulse oximetry (SpO₂) or by intermittent blood sampling to measure arterial oxygen tension (PaO₂) and saturation (Sao₂). Clinicians adjust parameters in response to these values by changing the inspired fraction of oxygen (FIO₂), the positive end-expiratory pressure (PEEP), and mean airway pressure.¹ Traditionally, this is done manually by clinicians at the bedside on an intermittent basis. In practice, these adjustments require a balance to avoid hypoxemia and hyperoxemia, both of which are associated with deleterious physiologic effects and increased mortality.^{2–5}

It can be challenging for clinicians to maintain normal arterial oxygen tension in critically ill and injured patients secondary to disease progression and physiologic demands. Likewise, traumatic injury and hemorrhage lead to dynamic systemic derangements that may require frequent ventilator changes to maintain appropriate levels of oxygenation. These difficulties are magnified when administering mechanical ventilation in austere environments where care personnel are limited and oxygen is a reduced resource. In these environments, computerized support systems based on algorithmic approaches to different phases of medical care may help mitigate the time demands of clinicians and lead to greater care efficiency and efficacy. Such support systems may use “decision assist” approaches, where the device synthesizes inputs from streaming patient data and presents the clinician with a best-practice recommendation. When these systems are applied to mechanical ventilation, closed-loop systems allow the ventilator to also act as a controller by comparing physiologic input data to goal values and making adjustments via feedback loops to bring the system closer to the predefined goal. To date, no studies have investigated the performance of closed-loop systems of oxygenation or ventilation in the setting of hemorrhagic shock and acute lung injury, a common injury pattern in austere, military, and mass-casualty environments.

In 1957, Saxton and Myers⁶ introduced the first system for closed-loop control of ventilation in which a goal end-tidal PCO₂ was used to drive changes in ventilator pressures. During the following decades, various closed-loop control systems were developed, but none demonstrated the stability necessary to transition effectively into clinical practice.⁷ Recent advances in microprocessors have allowed for multiple physiologic inputs to be concurrently analyzed, leading to greater stability for closed-loop algorithms. Preliminary laboratory and clinical studies from our group and others have demonstrated that recent improvements in closed-loop mechanical ventilation have reached a crucial threshold so that the algorithms

now seem applicable and safe for patient care during the course of routine critical care.^{8–12} As closed-loop mechanical ventilation strategies make their way into clinical practice, they will likely also be used in the care of nonroutine critically ill patients.

In the present study, we tested a portable ventilator modified with a closed-loop FIO₂ controller in a porcine model of combined hemorrhagic shock and acute lung injury. We hypothesized that the closed-loop controller would reliably maintain safe levels of oxygen saturation in both injured and uninjured animals.

MATERIALS AND METHODS

Animal Preparation and Mechanical Ventilation

All animal protocols were in accordance with the National Institutes of Health guidelines and were approved by the University of Cincinnati Institutional Animal Care and Use Committee. Twelve female Yorkshire pigs, with a mean (SD) weight 37.8 (3.2) kg, were obtained from a local vendor and allowed to acclimate in our facility for at least 48 hours. On the day of the procedure, they were sedated with intramuscular telazol (5 mg/kg) and xylazine (1 mg/kg), orotracheally intubated, positioned supine, and mechanically ventilated with a standard anesthesia ventilator (Ohmeda 7000, Ohmeda, Inc., Madison, WI) using standardized ventilator settings (FIO₂, 1.0; tidal volume (V_T), 10 mL/kg; PEEP, 5 cm H₂O; respiratory rate adjusted to achieve a target end-tidal carbon dioxide tension [P_{et}CO₂] of 35 [5] mm Hg). Anesthesia was maintained with inhaled isoflurane, while catheters were positioned as described later.

Instrumentation, Hemodynamic Monitoring, and Injury

All animals underwent cannulation of the following vessels: right femoral artery with a 20-gauge catheter (Teleflex Inc., Research Triangle Park, NC) for continuous blood pressure monitoring, right carotid artery with an 8.5 Fr catheter (Teleflex Inc., Research Triangle Park, NC) for hemorrhage and blood sampling, and right external jugular vein with a 7.5 Fr pulmonary artery (PA) catheter (Edwards Lifesciences, Irvine, CA) for the measurement of pulmonary capillary wedge pressure, cardiac output, central venous pressure, and PA pressure. After instrumentation was complete and baseline laboratory values were obtained, all pigs were transitioned to intravenous anesthesia (Propofol, 15–25 mg/kg/h, Abbott Animal Health, Abbott Park, IL) and converted to the portable ventilator (Impact 731, Impact Instrumentation, West Caldwell, NJ) with the standardized ventilator settings described earlier.

Pigs in the study group underwent a pressure-controlled hemorrhage by removing blood at 100 mL/min (Masterflex L/S pump, Cole Parmer, Vernon Hills, IL) to a mean arterial pressure (MAP) of 40 (5) mm Hg, and the volume of blood removed was recorded. This hypotensive state was actively maintained for 30 minutes followed by a passive 15-minute equilibration period.

An acute lung injury was induced with saline surfactant washout augmented with barotrauma, a modification of the technique used by Luecke et al.^{13,14} To achieve this, the ventilator circuit was disconnected, and up to 600 mL of warmed (37°C) normal saline was

instilled in 200-mL increments from a height of 50 cm. In between each instillation, the ventilator circuit was reconnected, and the animal was ventilated with a tidal volume of 7 mL/kg to 8 mL/kg and FIO₂ of 1.0 for 2 minutes to 3 minutes. After the full 600-mL volume was allowed to dwell for 2 minutes to 3 minutes, the saline was removed by gravity drainage, and the pig was reconnected to the ventilator circuit. The SpO₂ was allowed to return to baseline. The lavage was repeated until the SpO₂ remained lower than 92% after drainage of the saline (after approximately 3–4 L of saline wash). Following lung lavage, the ventilator mode was changed to pressure control with FIO₂ of 1.0, peak inspiratory pressure of 35 mm Hg, and PEEP of 0 to induce barotrauma. Respiratory rate was adjusted to maintain Paco₂ of 40 mm Hg to 50 mm Hg. Mechanical ventilation was continued for 1 hour, following which arterial blood gases were measured. Animals were determined to have lung injury and were included in the study if the PaO₂/FIO₂ ratio was less than 300. Included swine with lung injury (study group, n = 6) were ventilated for an additional 2 hours with the automated closed-loop control of FIO₂ algorithm (starting at an FIO₂ of 0.6, PEEP of 5 cm H₂O, V_T of 10 mL/kg, rate adjusted to maintain Paco₂ of 40–50 mm Hg). Animals in the sham group (n = 6) were maintained on standardized ventilator settings (FIO₂, 1.0; PEEP, 5 cm H₂O; V_T, 10 mL/kg; respiratory rate adjusted to maintain Paco₂ of 40–50 mm Hg) for 3 hours (the approximate time required to induce injury in the study group) before being switched to closed-loop control of FIO₂ for 2 hours. The time course of the study can be visualized in Figure 1.

Closed-Loop Control Ventilator Algorithm

The autonomous control algorithm is a modified negative feedback controller using an asymmetric gain that uses information regarding current FIO₂, current SpO₂, trend in SpO₂, and recent FIO₂ changes to maintain a target SpO₂ of 94% (2%). This information allows the controller to manipulate the FIO₂ with the rate of change determined by the degree of error or more simply, how far the SpO₂ is from the target. The maximum FIO₂ weaning rate is 2.88% per minute, and it slows down as the degree of error becomes smaller. A rule-based system controls algorithm behavior during periods of hypoxemia (defined as SpO₂ < 88% lasting for >10 seconds). Under these conditions, the increase in FIO₂ is more rapid with an immediate increase to 1.0 if hypoxemia persists.

Data Collection and Statistical Analysis

Blood samples for the measurement of pH, Paco₂, PaO₂, base excess, Sao₂, serum bicarbonate, lactate, hemoglobin, and hematocrit were collected at baseline, after hemorrhagic shock, after saline lavage, and then every hour during the observation period. Hemodynamic parameters (heart rate, MAP, central venous pressure, PA pressure) and SpO₂ were recorded manually from the monitor every 15 minutes. Pulmonary capillary wedge pressure and cardiac output were measured via the PA catheter every hour. Data collection software built into the closed-loop controller software recorded ventilator settings (FIO₂, V_T, PEEP, peak inspiratory pressure), heart rate, and SpO₂ values every 6 seconds during the autonomous control phase. At the completion of the procedure, animals were euthanized, and lung tissue was harvested for hematoxylin and eosin staining (Fig. 1).

SAS version 9.4 was used for statistical comparisons (SAS Institute Inc., Cary, NC). All data are presented as mean (SD) unless otherwise specified. Given the small sample size and nonnormal distribution of some variables, statistical comparisons between groups were made by Wilcoxon rank-sum test. Significance was defined as $p < 0.05$.

RESULTS

Sham and study pigs did not significantly differ in size or baseline hemodynamic values (heart rate, MAP, cardiac index). During the hemorrhage phase, study pigs lost a mean (SD) of 34.7% (8.4%) of their estimated total blood volume, representing a Class II to III hemorrhagic shock and resulting in a MAP that was significantly reduced in study versus sham animals at all time points except for baseline (Fig. 2A). Similarly, all study pigs had a $\text{PaO}_2/\text{FIO}_2$ ratio of less than 300 following the lung injury phase (mean [SD], 165 [86]). This decrease persisted throughout the duration of the autonomous control phase and was significantly reduced relative to baseline and to sham animals at corresponding time points (Fig. 2B). Gross examination of the lungs demonstrated markedly increased edema and hemorrhagic foci in study animals relative to shams, and histologic examination of the lungs showed increased septal wall thickening and edema in study lungs versus shams (Fig. 3). There was no significant difference between study and sham animals in any of the other hemodynamic parameters or laboratory values measured.

The FIO_2 was set at 1.0 during the instrumentation and injury phases for all animals and then started at 0.6 during the autonomous control phase. For all animals in the sham group, the controller weaned to an FIO_2 less than 0.5 within the first 15 minutes and remained less than 0.6 for the duration of the autonomous control phase. There was an overall trend of slow weaning to a final mean (SD) FIO_2 of 0.29 (0.1). The mean FIO_2 for the study animals was higher than shams at all time points during the autonomous control phase, but after an initial increase, there was still an overall decrease in FIO_2 for the study animals to a mean (SD) final FIO_2 of 0.54 (0.2). The controller responded to low SpO_2 ($< 92\%$) and made mean (SD) cumulative FIO_2 increases of 0.072 (0.08) in shams and 0.37 (0.2) in the study animals. There were four hypoxic episodes ($\text{SpO}_2 < 88$) that triggered immediate FIO_2 increase to 1.0 in the study group, and none of these episodes in the sham group. In spite of these differences in FIO_2 titration between the groups, there was no significant difference between the mean SpO_2 of the sham and study animals at any of the time points during the autonomous control phase (Fig. 4).

As described earlier, our closed-loop control algorithm is designed with a target SpO_2 of 94% (2%) with the clinical goal of avoiding both hypoxia ($\text{SpO}_2 < 88\%$) and hyperoxia ($\text{SpO}_2 > 97\%$). There was no significant difference between the sham and study animals in total time spent in a hypoxic state (0% [0%] vs. 1.9% [0.05%], $p = 0.18$), at target SpO_2 of 92% to 96% (42.6% [0.33%] vs. 34.3% [0.13%], $p = 0.688$), or in a hyperoxic state (57.4% [0.33%] vs. 56.5% [0.19%], $p = 0.348$) (Fig. 5).

DISCUSSION

In the present study, we examined the ability of a portable ventilator modified with a closed-loop FIO₂ controller to maintain oxygenation in a porcine model of hemorrhagic shock and acute lung injury. We found that the closed-loop controller responded to changes in SpO₂ with appropriate increases and decreases in FIO₂ and maintained the target SpO₂ range comparably in injured and uninjured animals. Automated closed-loop controllers of FIO₂ have existed in various forms for several decades. There is evidence in the literature that they can safely wean FIO₂ in healthy subjects and titrate oxygen in hemodynamically stable patients.^{15,16} Preliminary work by our group demonstrated significant reductions in oxygen use and hyperoxia in patients with closed-loop controlled versus clinician-controlled FIO₂.¹⁷ This work was performed on a heterogeneous civilian trauma population not controlled for the presence or degree of hemorrhage, hypotension, or lung injury. Similarly, recent studies of closed-loop control of FIO₂ and fully automated closed-loop ventilation in intensive care unit patients with acute respiratory failure, including those with adult respiratory distress syndrome, demonstrate safety and efficacy in maintaining oxygenation in the setting of significant lung injury.^{16,18} Given the key role of SpO₂ as a target for oxygenation in all of these systems and the known limitations of pulse oximetry in hypotension and shock states, we wanted to specifically study closed-loop control in the setting of hemorrhagic shock and lung injury.^{19,20} We used an updated version of the system used by Johannigman et al.⁹ to maintain the relevance for resource-limited critical care transport settings where the benefits of closed-loop control are magnified. We kept the target SpO₂ of 94% from this system because it falls within US Air Force Critical Care Air Transport Team standard of care guidelines for safe oxygen saturation and allows for weaning of FIO₂ when oxygen saturation is adequate.

Our autonomous controller performed comparably with others in the literature at preventing hypoxia.^{9,15,16} However, there were prolonged periods of hyperoxia during the autonomous control phase for almost all animals in the study (11 of 12 animals). This can potentially be attributed to several factors. The closed-loop algorithm that we used was designed to wean FIO₂ relatively slowly so as to mitigate an undershoot of the SpO₂ because of lung-to-pulse oximeter probe delay, leading to more time spent at a higher oxygen saturation. This finding may also represent a limitation of pulse oximetry. In all animals, but especially in study animals, it was common to have transient periods in which the plethysmograph waveform was attenuated or lost. An attenuated waveform generally registers as relative hypoxia, triggering increases in FIO₂ while a lost signal causes the algorithm to hold at the current FIO₂. These are safety features of the algorithm designed to prevent hypoxia, but such actions may inadvertently lead to hyperoxia. The clinical significance of these periods of hyperoxia is not well defined, and there is no evidence that a SpO₂ of 97% at a low FIO₂ incurs adverse effects. However, there is mounting evidence that administration of excess oxygen has toxic effects, even at levels that were previously considered safe.²¹ Oxygen is also a critical consumable resource in austere settings such as battlefield and disaster medicine.^{22,23} Our future work will focus on improving the efficiency of the closed-loop algorithm to minimize excess oxygen delivery and consumption while still preventing hypoxia.

The present study has several key limitations. Most importantly, it is an experimental large animal study. Even though our model has comparable respiratory mechanics to humans, swine have significant physiologic differences including contractile spleens and different coagulation profiles, which may alter responses to hemorrhage in ways that are not fully accounted for in our model. Second is the relatively mild level of hemorrhagic shock. Study pigs underwent a pressure-controlled hemorrhage and quantification of shed volumes correlated to either a Class II or Class III hemorrhagic shock. This was consistent with hemodynamic parameters seen in study versus sham pigs. MAP in the study pigs was significantly lower than that of the shams at all time points after baseline but was not significantly decreased from baseline. Similarly, heart rate and lactate increased in the study pigs after hemorrhage, while cardiac output and base excess decreased. However, these changes were not statistically different from the those of the shams or from baseline. During model development, a more severe hemorrhage was attempted, but the subsequent stress of inducing lung injury led to prohibitively high mortality. Thus, we cannot comment on the performance of our closed-loop controller in the setting of more severe hemorrhage. Third, it is important to note that we did not compare the performance of the closed-loop controller to standard ventilator management in the present study, which was designed primarily to determine feasibility and safety of the closed-loop FIO₂ controller in the setting of hemorrhage and lung injury. This comparison will be crucial to determine the efficacy and efficiency of this closed-loop system as this work goes forward. However, in the research setup of the present study, the research team (physician, respiratory therapist, and veterinary technician) was present at the bedside of the animal for the duration of the study. This is a significant variation from the standard clinical situation, and we felt that this would not give an accurate comparison to closed-loop control. Finally, the model in this study was designed with a low-level, fixed PEEP(5 cm H₂O) for all animals to eliminate the confounding effect of PEEP on oxygenation. This is in contradiction to clinical practice, particularly for patients with lung injury where increasing PEEP can improve oxygenation and enable a decrease in FIO₂. This is an important point because increased PEEP and resultant increased intrathoracic pressure may lead to decreased cardiac output and exacerbation of hypotension in a hypovolemic patient.²⁴ In addition to the adverse effects of systemic hypotension, this could obscure the SpO₂ signal, rendering the closed-loop controller ineffective. The combined effects of PEEP (both clinician-controlled and automated adjustments) and closed-loop control of FIO₂ in the setting of hemorrhagic shock are unclear and merit further investigation. Nonetheless, the findings of this study, together with the existing data regarding closed-loop control of oxygenation, suggest that automated closed-loop control of oxygenation is feasible in the setting of hemorrhage and lung injury. As such, it may represent a valuable tool for the care of traumatically injured patients, especially in resource-limited environments.

Acknowledgments

This study was funded by the Office of Naval Research grant #N00014-10-1-0252. R.D.B. has received honoraria from Cubist Pharmaceuticals and Ikaria.

References

1. Branson RD. The nuts and bolts of increasing arterial oxygenation: devices and techniques. *Respir Care*. 1993; 38:672–686. [PubMed: 10145847]
2. de Jonge E, Peelen L, Keijzers PJ, Joore H, de Lange D, van der Voort PH, Bosman RJ, de Waal RA, Wesselink R, de Keizer NF. Association between administered oxygen, arterial partial oxygen pressure and mortality in mechanically ventilated intensive care patients. *Crit Care*. 2008; 12(6):R156. [PubMed: 19077208]
3. Kilgannon JH, Jones AE, Shapiro NI, Angelos MG, Milcarek B, Hunter K, Parrillo JE, Trzeciak S. Association between arterial hyperoxia following resuscitation from cardiac arrest and in-hospital mortality. *JAMA*. 2010; 303:2165–2171. [PubMed: 20516417]
4. Altemeier WA, Sinclair SE. Hyperoxia in the intensive care unit: why more is not always better. *Curr Opin Crit Care*. 2007; 13:73–78. [PubMed: 17198052]
5. Strachan L, Noble DW. Hypoxia in surgical patients: prevention and treatment of an unnecessary cause of morbidity and mortality. *J R Coll Surg Edinb*. 2001; 46(5):297–302. [PubMed: 11697699]
6. Saxton GA Jr, Myers G. A servomechanism for automatic regulation of pulmonary ventilation. *J Appl Physiol*. 1957; 11(2):326–328. [PubMed: 13475186]
7. Tehrani FT. Automatic control of mechanical ventilation. Part 1: theory and history of the technology. *J Clin Monit Comput*. 22(6):417–424.
8. Branson RD. Modes to facilitate ventilator weaning. *Respir Care*. 2012; 57(10):1635–1648. [PubMed: 23013901]
9. Johannigman JA, Muskat P, Barnes S, Davis K, Branson RD. Autonomous control of oxygenation. *J Trauma*. 2008; 64(Suppl 4):S302–S320. [PubMed: 18385583]
10. Wysocki M, Jouve P, Jaber S. Closed loop mechanical ventilation. *J Clin Monit Comput*. 2014; 28(1):49–56. [PubMed: 23564277]
11. Wysocki M, Brunner JX. Closed-loop ventilation: an emerging standard of care? *Crit Care Clin*. 2007; 23(2):223–240. [PubMed: 17368167]
12. Lellouche F, Brochard L. Advanced closed loops during mechanical ventilation (PAV, NAVA, ASV, SmartCare). *Best Pract Res Clin Anaesthesiol*. 2009; 23(1):81–93. [PubMed: 19449618]
13. Luecke T, Meinhardt JP, Herrmann P, Weiss A, Quintel M, Pelosi P. Oleic acid vs. saline solution lung lavage-induced acute lung injury. *Chest*. 2006; 130(2):392–401. [PubMed: 16899837]
14. Matute-Bello G, Frevert CW, Martin TR. Animal models of acute lung injury. *Am J Physiol Lung Cell Mol Physiol*. 2008; 295:1379–1399.
15. Claude N, Bancalari E, D'Ugard C, Nelin L, Stein M, Ramanathan R, Hernandez R, Donn SM, Becker M, Bachman T. Multicenter crossover study of automated control of inspired oxygen in ventilated preterm infants. *Pediatrics*. 2011; 127(1):e76–e83. [PubMed: 21187305]
16. Saihi K, Richard JC, Gonin X, Kruger T, Dojat M, Brochard L. Feasibility and reliability of an automated controller of inspired oxygen concentration during mechanical ventilation. *Crit Care*. 2014; 18(1):R35. [PubMed: 24552490]
17. Johannigman JA, Branson RD, Lecroy D, Beck G. Autonomous control of inspired oxygen concentration during mechanical ventilation of the critically injured trauma patient. *J Trauma*. 2009; 66:386–392. [PubMed: 19204511]
18. Arnal JM, Garner A, Novonti D, Demory D, Ducros L, Berric A, Donati S, Corno G, Jaber S, Durand-Gasselin J. Feasibility study on full closed-loop control ventilation (IntelliVent-ASV™) in ICU patients with acute respiratory failure: a prospective observational comparative study. *Crit Care*. 2013; 17(5):R196. [PubMed: 24025234]
19. Talke P, Stapelfeldt C. Effect of peripheral vasoconstriction on pulse oximetry. *J Clin Monit Comput*. 2006; 20:305–309. [PubMed: 16841243]
20. Sinex JE. Pulse oximetry: principles and limitations. *Am J Emerg Med*. 1999; 17:59–67. [PubMed: 9928703]
21. Blakeman TC. Evidence for oxygen use in the hospitalized patient: is more really the enemy of good? *Respir Care*. 2013; 58(10):1679–1693. [PubMed: 24064627]

22. Blakeman TC, Branson RD. Oxygen supplies in disaster management. *Respir Care*. 2013; 58(1): 173–183. [PubMed: 23271827]
23. Barnes SL, Branson R, Gallo LA, Beck G, Johannigman JA. En-route care in the air: snapshot of mechanical ventilation at 37,000 feet. *J Trauma*. 2008; 64(2 Suppl):S129–S134. [PubMed: 18376155]
24. Fougères E, Teboul JL, Richard C, Osman D, Chemla D, Monnet X. Hemodynamic impact of a positive end-expiratory pressure setting in acute respiratory distress syndrome: importance of the volume status. *Crit Care Med*. 2010; 38:802–807. [PubMed: 19926983]

Figure 1.

Time course of the study is shown for the study animals and sham animals. Before T0m, all animals were sedated and intubated, and catheters were placed as described in the Materials and Methods section. Hemodynamic parameters were measured at indicated time points and every 15 minutes during the autonomous control phase.

Figure 2.

A, MAP (shown here indexed to baseline) was significantly decreased in the study animals relative to the shams at all time points following pressure-controlled hemorrhage ($p < 0.005$). B, Likewise, $\text{PaO}_2/\text{FIO}_2$ (P:F) ratio was less than 300 in the study animals following lung injury and was significantly lower than that of shams and baseline values at all time points ($p < 0.002$).

Figure 3. Necropsy specimens demonstrate increased edema and parenchymal hemorrhage in lungs from the study animals (*B*) relative to the shams (*A*). Representative sections from those same lungs stained with hematoxylin and eosin show normal alveolar structure in the shams (*C*) versus edema and alveolar wall thickening in the study animals (*D*).

Figure 4.

FiO₂ and SpO₂ are shown for the sham and study animals at baseline and for the autonomous closed-loop control phase of the study. FiO₂ was initially set at 0.6 for the autonomous control phase. There was a significantly lower FiO₂ in the shams relative to the study animals at all time points after the initiation of the closed-loop controller ($p < 0.05$). However, there was no significant difference in SpO₂ between the groups at any time point in the study.

Figure 5.

There was no significant difference between the sham (A) and study (B) groups in the percentage of time spent in different SpO₂ ranges. Neither group experienced any significant degree of hypoxemia (SpO₂ < 88%). However, both groups experienced prolonged periods of hyperoxemia (SpO₂ > 97%).