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## A Porcine Model for Initial Surge Mechanical Ventilator Assessment and Evaluation of Two Limited Function Ventilators

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### Abstract

**Objective**—To adapt an animal model of acute lung injury for use as a standard protocol for a screening, initial evaluation of limited function, or “surge,” ventilators for use in mass casualty scenarios.

**Design**—Prospective, experimental animal study.

**Setting**—University research laboratory.

**Subjects**—12 adult pigs.

**Interventions**—12 spontaneously breathing pigs (6 in each group) were subjected to acute lung injury/acute respiratory distress syndrome (ALI/ARDS) via pulmonary artery infusion of oleic acid. Following development of respiratory failure, animals were mechanically ventilated with a limited function ventilator (Simplified Automatic Ventilator [SAVE] I or II; Automedx) for one

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hour or until the ventilator could not support the animal. The limited function ventilator was then exchanged for a full function ventilator (Servo 900C; Siemens).

**Measurements and Main Results**—Reliable and reproducible levels of ALI/ARDS were induced. The SAVe I was unable to adequately oxygenate 5 animals, with PaO<sub>2</sub> (52.0 ± 11.1 torr) compared to the Servo (106.0 ± 25.6 torr; p=0.002). The SAVe II was able to oxygenate and ventilate all 6 animals for one hour with no difference in PaO<sub>2</sub> (141.8 ± 169.3 torr) compared to the Servo (158.3 ± 167.7 torr).

**Conclusions**—We describe a novel *in vivo* model of ALI/ARDS that can be used to initially screen limited function ventilators considered for mass respiratory failure stockpiles, and is intended to be combined with additional studies to definitively assess appropriateness for mass respiratory failure. Specifically, during this study we demonstrate that the SAVe I ventilator is unable to provide sufficient gas exchange, while the SAVe II, with several more functions, was able to support the same level of hypoxemic respiratory failure secondary to ALI/ARDS for one hour.

### Keywords

mass casualty incidents; ventilators, mechanical; acute lung injury; oleic acid; disaster medicine; respiratory distress syndrome, adult

## Introduction

Recent natural disasters, terrorist events, and the recent 2009 H1N1 influenza pandemic have compelled health care providers to consider the potential for mass respiratory failure. (1-5) No healthcare system currently has sufficient quantities of full-function critical care ventilators on hand for catastrophic needs.(5, 6) For scenarios such as a severe influenza pandemic, estimated shortfalls of mechanical ventilators are in the tens of thousands. Procurement and maintenance costs and logistical challenges prohibit stockpiles of sufficient quantities of full-function ventilators. Sophisticated transport ventilators with fewer functions than traditional intensive care unit ventilators have therefore been proposed by experts and professional societies as a “surge” ventilator supply in mass respiratory failure.(6, 7) Still, others believe that even more limited devices should be considered.(8-10) Many of these devices have technical and theoretical limitations,(11-13) yet their relatively low cost has led to early endorsement despite serious concerns regarding their capabilities. (11) To date there is not a standard approach for evaluating efficacy or effectiveness of surge mechanical ventilators.

At the minimum, a disaster mechanical ventilator should be capable of providing adequate gas exchange for the anticipated physiologic derangement. Most modern mass respiratory failure scenarios will likely lead to a surge of acute, hypoxemic respiratory failure or airflow obstruction. In most cases, hypoxemic respiratory failure due to ALI/ARDS would be the predominant conditions.(6, 14-17) The impact of a ventilator’s inability to deliver common respiratory parameters (e.g. respiratory rate, positive end expiratory pressure (PEEP), flow rate) to patients with ALI/ARDS remains uncertain.

In order to better evaluate “surge” ventilators, we describe a modification to a well-established porcine model of acute lung injury (18-21) that allows appropriate *in vivo* testing via simulation of acute hypoxemic respiratory failure with ALI/ARDS. We subsequently employ this model to test two new limited function ventilators that have been proposed for stockpiling. The ventilators, one of which has received Food and Drug Administration (FDA) approval for human use, have differing functional limitations. Neither has been previously tested using an animal model of lung injury.

## Materials and Methods

### Animal Preparation

All protocols were in accordance with the National Institutes of Health guidelines and were approved by the University of Washington Animal Care Committee and the Defense Department Animal Use Committee. Local community-bred pigs (n=12; 6 in each group; mean [ $\pm$ SD] weight  $24.7 \pm 2.9$  kg) were sedated intramuscularly with ketamine (25mg/kg) and xylazine (2.5 mg/kg) to allow ear vein cannulation. A surgical plane of anesthesia was obtained with an initial bolus of thiopental sodium (20mg/kg) and maintained with a continuous infusion (10-20 mg/kg/hr). Animals were mechanically ventilated via a tracheostomy (Servo 900C; Siemens-Eléma; Solna, Sweden) in the supine posture. Assist-controlled volume ventilation was adjusted to achieve a tidal volume ( $V_T$ ) of 8 to 10 ml/kg measured body weight, and respiratory rate was adjusted to achieve an end-tidal  $CO_2$  of 40 torr. PEEP was applied at 5 cm  $H_2O$ .

### Physiological Measurements

A femoral artery catheter was placed via cutdown for blood pressure measurement and arterial blood gas sampling. A femoral venous catheter was placed via cutdown for fluid and drug administration. An internal jugular catheter was placed via cutdown and a right heart catheter was advanced into the pulmonary artery to allow measurement of pulmonary artery pressure, pulmonary artery occlusion pressure (PAOP), mixed venous blood sampling, and administration of oleic acid. An esophageal balloon (Microtek Medical B.V., Zutphen, NL) was placed to measure esophageal pressure as a surrogate for pleural pressure. Body temperature was maintained between 36.0°C and 39.2°C using a heating pad.

Vascular pressures and esophageal pressures were measured intermittently (Mark 12 Data Management System, DMS 1000; Graphtec; Yokohama, Japan). Peak pressure,  $V_T$ , respiratory rate, and minute ventilation ( $V_E$ ) were continuously measured with an in-line spirometer (Medical KORR Technologies; Salt Lake City, UT) and end-tidal  $CO_2$ , heart rate, and transcutaneous  $O_2$  saturation were continuously monitored (CO2SMO; Novamatrix Medical System Inc; Wallingford, CT). Mean arterial blood pressure, pulmonary arterial pressure, esophageal pressure, peak airway pressure and  $V_T$  were digitally recorded on a personal computer (Power Lab data acquisition software; AD Instruments; Grand Junction, CO). Thermodilution cardiac outputs and core temperature were measured with a cardiac output computer (Sat-2, Baxter Edwards; Irvine, CA). Arterial and mixed-venous blood gases were analyzed at each experimental condition (ABL 5; Radiometer; Copenhagen, Denmark). Inspired  $O_2$  and mixed exhaled  $CO_2$  concentrations were measured with a spectrophotometer (MGA-1100; Perkin-Elmer Medical Instruments; Norwalk, CT).

All physiologic parameters were measured after 10 minutes of stabilization at baseline and under each experimental condition. Noninvasive measurements were monitored continuously.  $PaO_2/FiO_2$  ratios were calculated. Since end-inhalation pause was not possible with the SAVe ventilators, lung compliance was estimated as  $V_T/(P_{peak}-P_{esophageal})$ . Dead space fraction ( $V_D/V_T$ ) was estimated as  $(PaCO_2-P_{CO_2})/PaCO_2$ .

To prevent circulatory collapse, a continuous infusion of warmed Lactated Ringers solution (LR) was maintained throughout oleic acid delivery. Evidence of hypovolemia prior to lung injury (PAOP less than 6 mm Hg) was treated with up to 250 ml of LR to achieve a PAOP greater than 6 mm Hg. Hypotension during oleic acid infusion was treated with LR administration (up to 3L, excluding LR for pre-injury hypovolemia) and boluses of epinephrine at 10-20 mcg per bolus. Oleic acid infusion was held at any point where mean arterial pressure fell below 60 mm Hg and resumed when mean arterial pressure was greater than 80 mm Hg. Circulatory collapse was treated with closed chest compressions, bag mask

ventilation with  $F_{I}O_2$  of 1.0, and intravenous fluids (up to 3L total volume, including volume administered for hypotension) and administration of epinephrine (20-40 mcg/bolus).

## Ventilators

The Siemens 900C is a full feature ventilator [Table 1]. Its capabilities have been previously described.(22)

The Simplified Automated Ventilator I (SAVe I; Automedx; Germantown, MD) is a limited function ventilator [Table 1] with manufacturer set  $V_T$  and respiratory rate that is currently deployed with the United States Medical Corps and is available for purchase by medical and emergency medical services companies. The ventilator, as approved by the FDA for human use, has a set  $V_T$  of 600ml and respiratory rate of 10 breaths per minute. For the purposes of this study, the ventilator was adjusted by the manufacturer to achieve a respiratory rate of 40 breaths per minute with a  $V_T$  of approximately 210 ml due to the size of the animals being studied. Due to the potential risk of fire, the manufacturer recommended a limit of 6L/min oxygen entrainment. The ventilator is not capable of administering PEEP without use of an external PEEP valve.

The Simplified Automated Ventilator II (SAVe II; Automedx; Germantown, MD) is a second generation, limited function ventilator based on the SAVe I with the added capability of adjustable  $V_T$  and respiratory rate, entrainment of up to 15L/minute of  $O_2$ , and the ability to deliver and control PEEP (i.e. internal PEEP) [Table 1]. It has not received FDA approval at time of submission of this manuscript.

Both limited function ventilators have audible and visual alarms for circuit disconnect and high peak pressure. While the pressure alarm threshold is fixed on the SAVe I, it can be adjusted on the SAVe II. Both ventilators continue to deliver set  $V_T$  despite triggering peak pressure alarms. Neither ventilator is capable of ventilator triggering by patient inspiratory effort. Both ventilators have a battery power supply and are intended to be portable mechanical ventilators. For the purposes of this study, the ventilators were powered using their provided AC power adapters. Each ventilator requires a specific set of circuit and ancillary tubing which were used in accordance with manufacturer recommendations. Neither ventilator requires a compressed gas source.

## Lung Injury Protocol

In order to model acute respiratory failure, once surgical manipulation was complete and baseline values were obtained, continuous thiopental infusion was reduced until the animal was noted to breathe spontaneously while maintaining a deep plane of anesthesia (corresponding to a Richmond Agitation and Sedation Score (RASS) of -5). Baseline measurements were obtained and lung injury was accomplished via administration of 0.06 to 0.09 ml/kg oleic acid (O1630-25G; Sigma-Aldrich; St Louis, MO) via the proximal port of the right heart catheter with a goal to achieve lung injury as defined by a  $PaO_2/F_{I}O_2$  ratio of less than 300. Within each group, animals were randomly selected to receive oleic acid at either high, moderate, or low range of oleic acid to achieve a range of lung injury.

Due to change in availability of oleic acid during the course of the study, a purer form of oleic acid (O1008-25G; Sigma-Aldrich; St Louis, MO) was substituted for the second half of the study. Following this substitution of oleic acid, we witnessed a decrease in lung injury obtained (as measured by  $PaO_2/F_{I}O_2$  ratio); therefore, the dose of oleic acid was increased to 1.0-1.25 ml/kg for the second set of 6 pigs. Oleic acid infusion was performed in the same manner.

To minimize systemic hypotension during oleic acid infusion, oleic acid was diluted into saline to achieve 20 ml total infused volume. Due to the hydrophobic nature of oleic acid, 1 ml of air was also introduced into the glass syringe to facilitate mixing of the oleic acid with saline. A vortex machine (Maxi Mix II; Thermolyne; Dubuque, IA) kept the oleic acid mixed with the saline while being administered. Oleic acid was administered by hand injection over a 10 to 20 minute period. Following infusion, the catheter was flushed with saline to ensure all of the oleic acid was administered.

### Experimental Protocol

Each animal was ventilated with the Siemens 900C, followed by the SAVe I (first 6 animals) or SAVe II (second 6 animals) prior to lung injury. The ventilators were tested independently with sequential groups of pigs. Following baseline data acquisition, anesthesia was decreased until sustained spontaneous ventilation was noted, and lung injury was established [Figure].

Following lung injury, spontaneous breathing animals were monitored for evidence of respiratory failure: respiratory rate greater than 50 or less than 20 breaths per minute, SpO<sub>2</sub> less than 80% despite administration of 100% O<sub>2</sub>, apnea, or cardiac arrest. Following spontaneous respiratory failure, the SAVe ventilator was used to provide respiratory support and anesthesia was returned to a surgical plane (RASS -5) by increasing the infusion rate of thiopental.

Support was continued with the SAVe ventilator until evidence of respiratory failure was noted: SpO<sub>2</sub> less than 80% despite maximal oxygen and PEEP delivery (if PEEP was able to be delivered), PaCO<sub>2</sub> greater than 80 torr, or PaO<sub>2</sub> less than 45 torr. Once respiratory failure was noted, the Servo 900C was substituted and adjustments were made to correct any noted physiologic deficits while targeting V<sub>T</sub> of 6ml/kg. As peak injury from oleic acid occurs one hour following infusion,(23) the animal was supported with the SAVe for one hour if respiratory failure did not develop, and then transitioned to the Servo 900C.

Since the SAVe I was not capable of delivering PEEP, increased F<sub>I</sub>O<sub>2</sub> was used as the primary method for treating hypoxemia with all ventilators; PEEP could be added for refractory hypoxia, however, while on the Servo. When transitioning from the SAVe II to the Servo, PEEP was initially applied at the same level provided by the SAVe II. This could then be titrated to maintain appropriate oxygen saturations.

### Statistical Analysis

Values are reported as mean ± standard deviation. Statistical analyses were performed using STATA version 10 for Windows (StataCorp LP, College Station, TX, USA). T-tests were used to compare continuous variables. A p value <0.05 was used to determine statistical significance.

## Results

### Save I

There was no difference in PaO<sub>2</sub> or PaO<sub>2</sub>/F<sub>I</sub>O<sub>2</sub> ratio at baseline whether ventilated by Servo or SAVe I [Table 2]. However, PaCO<sub>2</sub> was lower while undergoing baseline ventilation with the SAVe I and V<sub>E</sub> was greater. Lung compliance tended to be greater during baseline ventilation on the Servo, though this difference was not statistically significant. There was no difference in baseline mean systemic blood pressure, pulmonary artery pressure, or cardiac output.

One of six animals suffered cardiac arrest during oleic acid infusion but was resuscitated and the experiment was completed. All animals were included in the final analysis. Doses of oleic acid ranged from 0.06 ml/kg to 0.09 ml/kg with a median dose of 0.08 ml/kg. The degree of lung injury varied between animals with  $\text{PaO}_2/\text{F}_1\text{O}_2$  ratio ranging from 91 to 288 (median 129). Measured dead space fraction (measured while ventilated on the Siemens) increased from  $0.49 \pm 0.06$  pre-injury to  $0.68 \pm 0.09$  after injury ( $p=0.003$ ), while measured compliance decreased from  $21.3 \pm 9.0$  ml/cm  $\text{H}_2\text{O}$  to  $8.8 \pm 1.9$  ml/cm  $\text{H}_2\text{O}$  ( $p=0.03$ ) following lung injury.

The SAVe I ventilator was capable of supporting only one of the six animals after development of acute lung injury. For the remaining five animals, the SAVe I was not capable of maintaining measured oxygen saturation greater than 80% for at least one hour after completion of oleic acid infusion. In contrast, the Siemens Servo 900C was capable of maintaining specified clinical variables in all 6 animals.  $\text{PaO}_2$  was lower while being ventilated with the SAVe I ventilator compared to the Servo [Table 3]. The decrease in  $\text{PaO}_2$  coincided with a lower  $\text{F}_1\text{O}_2$  and PEEP, although the difference in  $\text{F}_1\text{O}_2$  delivered was not statistically significant. There was no statistically significant difference in  $\text{PaO}_2/\text{F}_1\text{O}_2$  ratio,  $\text{PaCO}_2$ ,  $\text{V}_E$ , pulmonary compliance, peak airway pressure, mean systemic blood pressure, mean pulmonary artery pressure, PAOP, or cardiac output when ventilated with the SAVe I or Siemens Servo.

## SAVe II

There was no difference in  $\text{PaO}_2$ ,  $\text{PaCO}_2$ ,  $\text{V}_E$ , or  $\text{PaO}_2/\text{F}_1\text{O}_2$  ratio at baseline whether ventilated by Servo or SAVe II [Table 2]. Measured lung compliance tended to be greater during baseline ventilation on the Servo while peak airway pressures were greater while being ventilated with the SAVe II. There was no difference in baseline mean systemic blood pressure, pulmonary artery pressure, PAOP or cardiac output.

Doses of oleic acid ranged from 0.090 ml/kg to 0.125 ml/kg with a median dose of 0.124 ml/kg. The degree of lung injury varied between animals with  $\text{PaO}_2/\text{F}_1\text{O}_2$  ratio ranging from 97 to 303 (median 193), with one animal not achieving lung injury. Measured dead space (measured while ventilated on the Servo) increased from  $0.47 \pm 0.04$  pre-injury to  $0.64 \pm 0.13$  after injury ( $p=0.02$ ), while measured compliance decreased from  $27.8 \pm 10.4$  ml/cm  $\text{H}_2\text{O}$  to  $10.4 \pm 4.1$  ml/cm  $\text{H}_2\text{O}$  ( $p=0.008$ ) following lung injury.

The SAVe II ventilator was capable of supporting all six animals for at least one hour after development of acute lung injury based on pre-specified clinical requirements using lung protective ventilation and permissive hypercapnia. There was no statistically significant difference in measured  $\text{PaO}_2$ ,  $\text{PaCO}_2$ ,  $\text{V}_E$ , compliance,  $\text{PaO}_2/\text{F}_1\text{O}_2$  ratio, PAOP, cardiac output, peak airway pressure, PEEP,  $\text{F}_1\text{O}_2$ , mean systemic blood pressure, or pulmonary artery pressure when ventilated with the SAVe II or the Servo [Table 4].

There was no difference in lung compliance,  $\text{PaO}_2/\text{F}_1\text{O}_2$  ratio, measured dead space fraction, or peak airway pressure between the two groups of pigs at the start of the experiment or at the end of the experiment (as measured while being ventilated with the Siemens Servo 900C).

## Discussion

We demonstrated the utility of an oleic acid model of acute lung injury modified to replicate acute hypoxemic respiratory failure allowing initial screening of limited function ventilators that might be stockpiled for mass respiratory failure events. Using this model, we demonstrated that the limited-feature device (SAVe I) was unable to adequately oxygenate

animals even for a short period of time, while the additional features of the SAVe II allowed successful short-term ventilation and oxygenation despite severe lung injury. The SAVe I's failure was likely due to ventilator limitations rather than extreme levels of respiratory failure, as the same animals were able to be "rescued" using a Servo 900C and supplemental oxygen. Although there was a wide range of variability in the degree of acute lung injury obtained, by using a cross-over design we were able to demonstrate that the SAVe I was not capable of supporting any level of lung injury for one hour, while the Servo was able to support a similar degree of lung injury. No significant difference in  $\text{PaO}_2/\text{FiO}_2$  ratio was present in the animals at peak lung injury or respiratory failure when ventilated by the SAVe I ventilator or Servo; the non-significant difference that was observed likely reflects the difference in PEEP between the two groups more than a difference in the severity of lung injury.

The respiratory alkalosis observed in the animals on the SAVe I ventilator prior to lung injury is a consequence of the fixed respiratory rate and tidal volume on the device. These parameters were set by the manufacturer in anticipation of the ventilatory needs of the animal after lung injury. This highlights the importance of adjustable rate and tidal volume on a limited-function surge ventilator, which should be capable of providing ventilation to patients with varying degrees of lung injury.

In this experiment, the FDA-approved SAVe I, a device with a compressor capable of flows of 16 L/min and with a fixed respiratory rate and tidal volume, was unable to adequately oxygenate a porcine model of oleic acid induced acute lung injury. In contrast, the SAVe II ventilator, which incorporates a compressor capable of flow at 80 L/min, adjustable  $V_T$  and respiratory rate, and the ability to deliver  $\text{F}_1\text{O}_2$  up to 1.0 and maintain PEEP, was able to both oxygenate and ventilate the pigs for up to one hour. Despite similar lung injury between the SAVe I and the SAVe II groups, there was no evidence of failure of the SAVe II over the course of one hour. This difference is likely attributable to the SAVe II's ability to provide higher levels of  $\text{F}_1\text{O}_2$  and PEEP than could be provided by the SAVe I. This provides experimental support for expert statements that "surge" ventilators should be able to provide PEEP.(7, 15, 16)

Some disaster planners have proposed that limited feature ventilators be used as an initial device until patients with worsening respiratory failure require ventilators with additional features. The epidemiology of mechanical ventilation requirements for critically ill medical patients does not support this stepwise expectation. For such patients, where respiratory failure progresses to require mechanical ventilation, the initial settings are usually quite severe.(24, 25) The protocol in this study was developed to accurately mimic the typical early course of ALI/ARDS in previously spontaneously breathing subjects.(26, 27)

Although some have argued that few disaster victims who require respiratory failure will have ALI/ARDS, this has not born out in clinical studies or recent experience.(28) The majority of H5N1 patients with respiratory failure have ARDS,(29, 30) as do patients with seasonal flu(31) or H1N1 influenza.(32-36) Hence, we believe that our model, which allows for titration of  $\text{PaO}_2/\text{F}_1\text{O}_2$  abnormalities across a range of lung injury, has utility for initially evaluating surge mechanical ventilators. In fact, in light of reports of very severe ARDS with  $\text{PaO}_2/\text{F}_1\text{O}_2$  less than 100 in patients with respiratory failure due to novel H1N1, this model could be titrated to screen out inadequate devices. We acknowledge that some of the limited function devices will be allocated to lesser ill patients, patients improving and patients ventilated for reasons other than pulmonary pathology (e.g. traumatic brain injury). Yet the ability for these devices to have some utility for the predominant cause of the mass respiratory failure remains a logical requirement for stockpiling.

Of note, while the features of the SAVe II ventilator are more compatible with those of the ARDSnet ventilatory protocol (24) than the SAVe I device (permitting greater respiratory rate, PEEP settings, and adjustable tidal volumes), the device is not fully capable of the protocol's requirements. Specifically, its maximum respiratory rate, its maximum PEEP, the lack of adjustable inspiratory:expiratory duration or flow and the lack of plateau pressure monitors all limit its ability to match the protocol's requirements. Moreover, the device is capable only of Controlled Mechanical Ventilation, not Volume Assist-Control Ventilation as directed by the protocol; this limitation would likely mandate either paralysis or high levels of sedation for patients.

Currently, there is no standard against which to evaluate limited function or "surge" ventilators. While expert opinion has offered suggestions for minimal functional capabilities, there is no consensus. Some ventilators with fewer features and limited clinical data continue to be endorsed for use in stockpiling.(8, 37) Animal models of acute lung injury such as ours can provide a rapid assessment of minimal ventilator capabilities to target which limited function ventilators warrant further testing for use in clinical settings.

Although limited function ventilators are less expensive than full function ventilators, we believe that clinical requirements must determine the correct testing standards. While some have offered the polio epidemic of the 1950's as evidence that patients suffering respiratory failure can be supported with limited supportive techniques, such patients suffered from neuromuscular failure rather than parenchymal lung disease.(16) Similarly, groups have published data suggesting a single ventilator could ventilate several patients,(8) although this method has not been adequately tested in the setting of lung injury.(10)

Our *in vivo* model has limitations. The ventilators were only tested for a short duration, a function of the natural course of oleic acid-induced lung injury. The animals had limited spontaneous breathing once respiratory failure ensued (RASS -5); they were therefore not challenged with ventilator dyssynchrony as commonly seen in humans with respiratory failure who retain a spontaneous ventilatory drive. This model is better equipped to assess ventilators' ability to support hypoxemic respiratory failure than hypercapnic respiratory failure. Lastly, there was no noticeable airflow obstruction, which could require higher flow rates than achievable by some limited feature devices. Although our model may have utility in excluding proposed limited function ventilators for stockpiling, further testing for a longer duration is warranted prior to decisions to procure such devices on a large scale. Additionally, we believe that *in vivo* protocols should be established to mimic anticipated needs for spontaneously breathing patients, airflow obstruction, and severely ill pediatric patients in addition to longer term testing of ventilators that pass an initial evaluation.

Our protocol can be used as a screen so that devices with very limited utility are not purchased for mass respiratory failure stockpiles. However, further evaluation, including human testing, would still be necessary to prove clinical utility for devices that passed initial screening tests.

## Conclusion

We describe a novel *in vivo* model of ALI/ARDS that can be used to initially screen limited function ventilators considered for mass respiratory failure stockpiles. We demonstrate that the SAVe I ventilator is unable to provide sufficient gas exchange, while the SAVe II ventilator is able to support a comparable level of hypoxemic respiratory failure secondary to ALI/ARDS for one hour. We recommend further study assessing longer duration and different etiologies and aspects of respiratory failure prior to large-scale procurement of these devices.



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David Hotchkin developed the protocol, performed the experiments and was a writer of this manuscript.

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Lewis Rubinson conceived of the project, developed the protocol, assisted with some of the experiments and was a major contributor to the manuscript.

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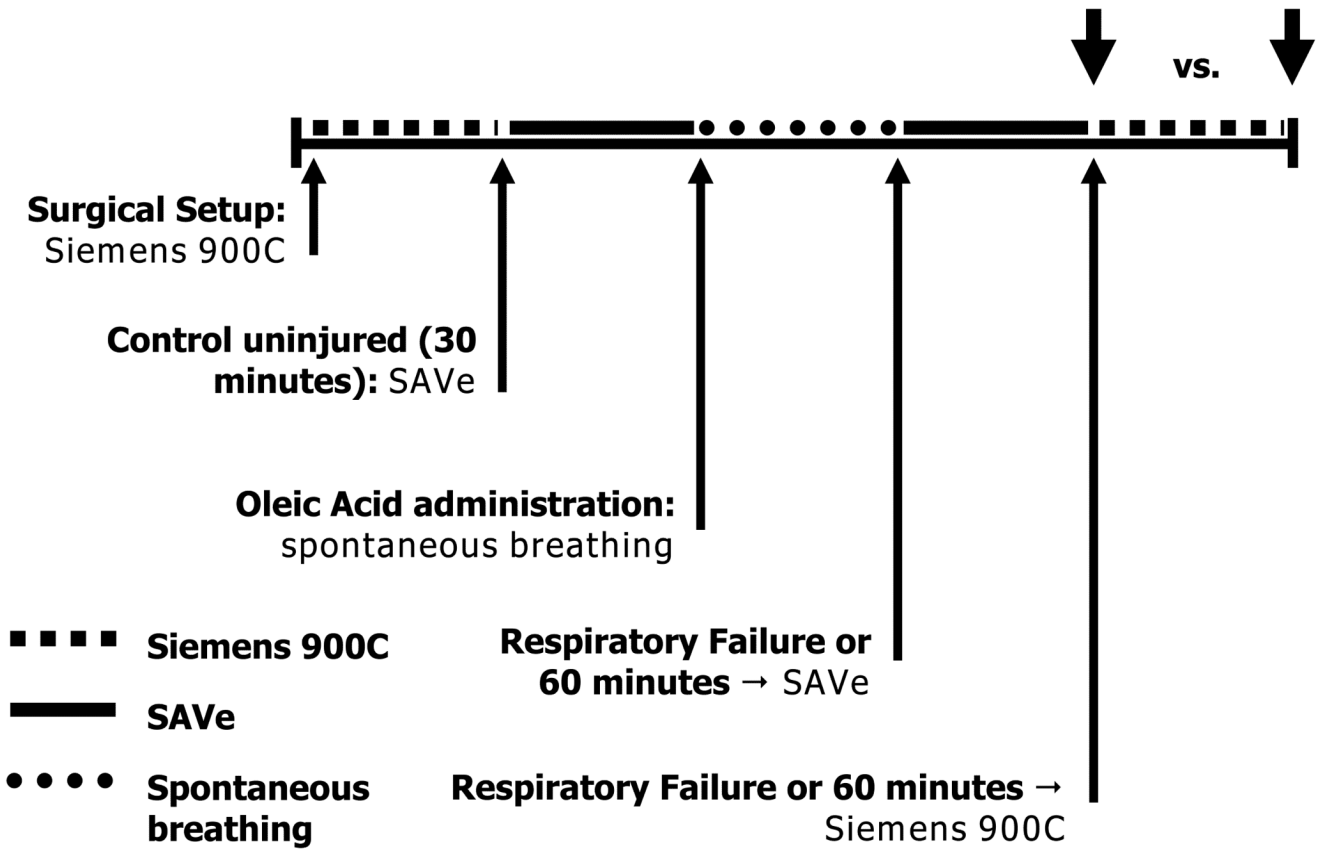
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**Figure. Flow diagram of experimental model**

Each animal was initially ventilated while baseline data was obtained. Anesthesia was then lightened to allow for spontaneous respirations. Lung injury was then induced. Pigs continued to breathe spontaneously until respiratory failure when they were moved to SAVE ventilator. Upon failure of the SAVE ventilator, or after a one hour period, they were ventilated with the Siemens Servo 900C. Comparisons of ventilator capability to support each pig was made at the end of each time period (Large arrows).

**Table 1**  
**Comparison of ventilator features.**

Feature	SAVe I	SAVe II	Servo
$V_T$	Fixed (0.6 L)	Variable (0.2 – 1 L)	Variable (0 – 2L)
Respiratory Rate (breaths per minute)	10	8-20	5-120
PEEP (cm H <sub>2</sub> O)	0	0-20	0-50
PIP (cm H <sub>2</sub> O)	Up to 38	Up to 60	0-100
Inspiratory flow (L/min)	16	10-80	Adjustable to a maximum of 200
Breath type	Volume	Volume	Volume, Pressure
Weight (kg)	1.4	1.4	19
Power	AC, Battery	AC, Battery	AC
Battery Life (hours)	5.5	6.5	NA
Price (US Dollars)	\$1,695	\$1,995	Not available

Reported features for the Siemens Servo,(38) and the SAvE I & II (Personal communication, Automedx, Nov. 26, 2008)

**Table 2**  
**Baseline measured physiologic parameters for ventilation with the SAVe I, SAVe II, or Siemens Servo 900C.**

Variable	SAVe I(n=6)		SAVe II (n=6)	
	Servo	SAVe I	Servo	SAVe II
<b>PaO<sub>2</sub>, torr</b>	92.5 ± 9.1	92.5 ± 14.1	96.3 ± 3.7	98.5 ± 6.3
<b>PaCO<sub>2</sub>, torr</b>	37.7 ± 1.8 <sup>*</sup>	27.7 ± 4.2 <sup>*</sup>	38.3 ± 2.9	36.5 ± 3.1
<b>V<sub>E</sub>, L/min</b>	5.7 ± 1.5 <sup>†</sup>	8.3 ± 0.8 <sup>†</sup>	5.3 ± 1.6	5.1 ± 1.3
<b>Peak airway pressure, cm H<sub>2</sub>O</b>	16.7 ± 2.1	14.7 ± 3.4	16.9 ± 2.3 <sup>§</sup>	20.5 ± 2.5 <sup>§</sup>
<b>Compliance, ml/cm H<sub>2</sub>O</b>	21.3 ± 9.0	15.6 ± 5.2	27.8 ± 10.4 <sup>‡</sup>	16.8 ± 3.0 <sup>‡</sup>
<b>PaO<sub>2</sub>/F<sub>I</sub>O<sub>2</sub> ratio</b>	440.5 ± 43.2	440.5 ± 67.1	458.7 ± 17.5	463.9 ± 24.0
<b>Mean BP, mm Hg</b>	106.5 ± 9.8	99.8 ± 13.9	97.7 ± 10.2	97.7 ± 7.3
<b>Mean pulmonary artery pressure, mm Hg</b>	17.5 ± 3.0	15.6 ± 3.3	15.6 ± 2.6	15.9 ± 2.3
<b>Cardiac Output, L/min</b>	2.47 ± 0.40	2.83 ± 0.60	2.58 ± 0.62	2.79 ± 0.57
<b>PAOP</b>	7.63 ± 0.98 <sup>+</sup>	5.83 ± 0.98 <sup>+</sup>	7.50 ± 1.87	7.42 ± 2.11

Values are mean ± SD. Comparisons are made between Siemens Servo and SAVe ventilator in each group. p>0.05 unless specified.

\* p=0.001

† p=0.007

§ p=0.02

‡ p=0.048

+ p=0.01.

**Table 3**  
**Physiologic variables at failure of mechanical ventilation or peak lung injury while being supported with SAVe I or Siemens 900C. (n=6)**

Variable	Servo	SAVe I
PaO <sub>2</sub> , torr	106.0 ± 25.6 *	52.0 ± 11.1 *
PaCO <sub>2</sub> , torr	57.8 ± 11.3	56.3 ± 19.7
V <sub>E</sub> , L/min	5.9 ± 2.0	5.5 ± 1.1
Compliance, ml/cm H <sub>2</sub> O	8.8 ± 1.9	5.9 ± 2.9
PaO <sub>2</sub> /F <sub>I</sub> O <sub>2</sub> ratio	147.2 ± 71.1	93.2 ± 33.2
Mean BP, mm Hg	97.3 ± 18.4	106.7 ± 25.9
Mean pulmonary artery pressure, mm Hg	35.1 ± 9.1	46.7 ± 17.2
Cardiac Output, L/min	1.55 ± 0.53	1.71 ± 0.51
PAOP, mm Hg	12.50 ± 4.04	14.30 ± 6.06
PEEP, cm H <sub>2</sub> O	6.7 ± 3.2 †	0 †
F <sub>I</sub> O <sub>2</sub>	0.80 ± 0.25	0.58 ± 0.06
Peak airway pressure, cm H <sub>2</sub> O	30.8 ± 7.2	29.5 ± 6.9

Values are mean ± SD. Comparisons are made between Siemens Servo and SAVe I ventilator. p>0.05 unless specified.

\* p=0.002

† p=0.003.

**Table 4**  
**Physiologic variables at failure of mechanical ventilation or peak lung injury while being supported with SAVe II or Siemens 900C. (n=6)**

Variable	Servo	SAVe II
PaO <sub>2</sub> , torr	158.3 ± 167.7	141.8 ± 169.3
PaCO <sub>2</sub> , torr	58.5 ± 17.0	52.5 ± 10.4
V <sub>E</sub> , L/min	5.2 ± 1.4	5.0 ± 1.3
Compliance, ml/cm H <sub>2</sub> O	10.4 ± 4.1	8.6 ± 3.8
PaO <sub>2</sub> /F <sub>I</sub> O <sub>2</sub> ratio	244.2 ± 140.8	224.8 ± 145.8
Mean BP, mm Hg	94.5 ± 22.5	90.8 ± 22.0
Mean pulmonary artery pressure, mm Hg	32.2 ± 5.4	32.7 ± 4.0
Cardiac Output, L/min	2.04 ± 0.72	2.03 ± 0.75
PAOP, mm Hg	10.58 ± 3.77	11.50 ± 4.85
PEEP, cm H <sub>2</sub> O	7.7 ± 2.6	5.7 ± 1.2
F <sub>I</sub> O <sub>2</sub>	0.61 ± 0.30	0.58 ± 0.30
Peak airway pressure, cm H <sub>2</sub> O	31.7 ± 7.3	36.2 ± 10.8

Values are mean ± SD. Comparisons are made between Siemens Servo and SAVe II ventilator. p>0.05 for all comparisons.