A porcine model for initial surge mechanical ventilator assessment and evaluation of two limited-function ventilators

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Objectives: 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: Twelve adult pigs.

Interventions: Twelve spontaneously breathing pigs (six in each group) were subjected to acute lung injury/acute respiratory distress syndrome via pulmonary artery infusion of oleic acid. After development of respiratory failure, animals were mechanically ventilated with a limited-function ventilator (simplified automatic ventilator [SAVe] I or II; Automed, Germantown, MD) for 1 hr or until the ventilator could not support the animal. The limited-function ventilator was then exchanged for a full-function ventilator (Servo 900C; Siemens-Elema, Solna, Sweden).

Measurements and Main Results: Reliable and reproducible levels of acute lung injury/acute respiratory distress syndrome were induced. The SAVe I was unable to adequately oxygenate five animals with Pao₂ (52.0 ± 11.1 torr) compared to the Servo (106.0 ± 25.6 torr; p = .002). The SAVe II was able to oxygenate and ventilate all six animals for 1 hr with no difference in Pao₂ (141.8 ± 168.3 torr) compared to the Servo (158.3 ± 167.7 torr).

Conclusions: We describe a novel in vivo model of acute lung injury/acute respiratory distress syndrome that can be used to initially screen limited-function ventilators considered for mass respiratory failure stockpiles and that 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, whereas the SAVe II, with several more functions, was able to support the same level of hypoxic respiratory failure secondary to acute lung injury/acute respiratory distress syndrome for 1 hr. (Crit Care Med 2011; 39:S27-S32)

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

Recent natural disasters, terrorist events, and the recent 2009 H1N1 influenza pandemic have compelled healthcare providers to consider the potential for mass respiratory failure (1–5). No healthcare system currently has sufficient quantities of full-function critical care ventilators 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 therefore have 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 hypoxic respiratory failure or air flow obstruction. In most cases, hypoxic respiratory failure attributable to acute lung injury/acute respiratory distress syndrome (ALI/ARDS) would be the predominant condition (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.

To better evaluate surge ventilators, we describe a modification to a well-established porcine model of ALI (18–21) that allows appropriate in vivo testing via
simulation of acute hypoxic respiratory failure with ALI/ARDS. We subsequently use 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 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; six in each group; mean 1 ± 20) weight 24.7 ± 2.9 kg) were sedated intramuscularly with ketamine (25 mg/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 (20 mg/kg) and maintained with a continuous infusion (10–20 mg/kg/hr). Animals were mechanically ventilated via a tracheostomy (Servo 900C; Siemens-Elema, Solna, Sweden) in the supine position. Assist-controlled volume ventilation was adjusted to achieve a tidal volume (V_t) of 8–10 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.

**Physiologic Measurements.** A femoral artery catheter was placed via cut-down for blood pressure measurement and arterial blood gas sampling. A femoral venous catheter was placed via cut-down for fluid and drug administrations. An internal jugular catheter was placed via cut-down 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 (Microtect Medical B.V., Zutphen, The Netherlands) 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; Graphitem, 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; Novametrix Medical System, 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). Thermoelectric 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 expired CO_2 concentrations were measured with a spectrophotometer (MGA-1100; Perkin-Elmer Medical Instruments, Norwalk, CT).

All physiologic parameters were measured after 10 min of stabilization at baseline and under each experimental condition. Noninvasive measurements were monitored continuously. PAOP or PAO/Fio_2 ratios were calculated. Because end-inspiration pause was not possible with the simplified automated ventilator I and II (SAVe; Automedex, Germantown, MD), lung compliance was estimated as V_t/(P_{peak} - P_{esophageal}). Dead space fraction (Vd/VT) was estimated as (P_{cO_2} - P_{cO_2})/(P_{cO_2} - P_{cO_2}).

To prevent circulatory collapse, a continuous infusion of warmed lactated Ringers solution was maintained throughout oleic acid delivery. Evidence of hypovolemia before lung injury (PAOP <6 mm Hg) was treated with up to 250 ml of lactated Ringers solution to achieve PAOP >6 mm Hg. Hypotension during oleic acid infusion was treated with lactated Ringers solution administration (up to 3 L, excluding lactated Ringers solution for pre-injury hypovolemia) and boluses of epinephrine at 10–20 μg per bolus. Oleic acid infusion was held at any point when mean arterial pressure decreased to <60 mm Hg and was resumed when mean arterial pressure was >80 mm Hg. Circulatory collapse was treated with closed chest compressions, bag mask ventilation with FIO_2 of 1.0, intravenous fluids (up to 3 L total volume, including volume administered for hypotension) and administration of epinephrine (20–40 μg bolus).

**Ventilators.** The Siemens 900C is a full-featured ventilator (Table 1). Its capabilities have been previously described (22).

The SAVe I is a limited-function ventilator (Table 1) with manufacturer-set V_t and respiratory rate that is currently deployed with the U.S. Medical Corps and is available for purchase by medical and emergency medical services companies. The ventilator, as approved by the Food and Drug Administration for human use, has a set V_t of 600 ml 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 because of the size of the animals being studied. Because of the potential risk of fire, the manufacturer recommended a limit of 6 L/min oxygen entrainment. The ventilator is not capable of delivering PEEP without use of an external PEEP valve.

The SAVe II 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 15 L/min of O_2, and the ability to deliver and control PEEP (i.e., internal PEEP) (Table 1). It has not received Food and Drug Administration approval at time of submission of this article.

Both limited-function ventilators have audible and visual alarms for circuit disconnect and high peak pressure. Although 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 ca-
pable 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 alternating current power adapters. Each ventilator requires a specific set of circuit and ancillary tubing that were used in accordance with manufacturer recommendations. Neither ventilator requires a compressed gas source.

**Lung Injury Protocol.** To model acute respiratory failure, once surgical manipulation was complete and baseline values were obtained, continuous thoracic 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 of −5). Baseline measurements were obtained and lung injury was accomplished via administration of 0.06–0.09 mL/kg oleic acid (01639-25G; Sigma-Aldrich, St. Louis, MO) via the proximal port of the right heart catheter with a goal of achieving lung injury as defined by a PaO₂/FIO₂ ratio of <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.

Because of change in availability of oleic acid during the course of the study, a purer form of oleic acid (01008-225G; Sigma-Aldrich) was substituted for the second half of the study. After this substitution of oleic acid, we witnessed a decrease in lung injury obtained (as measured by PaO₂/FIO₂ ratio); therefore, the dose of oleic acid was increased to 1.0–1.25 mL/kg for the second set of six 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. Because of 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 manual injection over a 10- to 20-min period. After infusion, the catheter was flushed with saline to ensure that all of the oleic acid was administered.

**Experimental Protocol.** Each animal was ventilated with the Siemens 900C, followed by the SAVe I (first six animals) or SAVe II (second six animals) before lung injury. The ventilators were tested independently with sequential groups of pigs. After baseline data acquisition, anesthesia was decreased until sustained spontaneous ventilation was noted and lung injury was established (Fig. 1). After lung injury, spontaneously breathing animals were monitored for evidence of respiratory failure: respiratory rate >50 or <20 breaths per minute, SpO₂ <80% despite administration of 100% O₂, apnea, or cardiac arrest. After spontaneous respiratory failure, the SAVe ventilator was used to provide respiratory support and anesthesia was returned to a surgical plane (Richmond Agitation and Sedation Score −5) by increasing the infusion rate of thiopental.

Support was continued with the SAVe ventilator until evidence of respiratory failure was noted: SpO₂ <80% despite maximal oxygen and PEEP delivery (if PEEP was able to be delivered), PaCO₂ >80 torr, or PaO₂ <45 torr. Once respiratory failure was noted, the Servo 900C was substituted and adjustments were made to correct any noted physiologic deficits while targeting Vt of 6 mL/kg. Because peak injury from oleic acid occurs 1 hr after infusion (23), the animal was supported with the SAVe for 1 hr if respiratory failure did not develop and then transitioned to the Servo 900C.

Because the SAVe I was not capable of delivering PEEP, increased FIO₂ was used as the primary method for treating hypoxemia with all ventilators; PEEP could be added for refractory hypoxia, however, while using 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 ± so. Statistical analyses were performed using STATA version 10 for Windows (StataCorp LP, College Station, TX). t tests were used to compare continuous variables. A p < .05 was used to determine statistical significance.

![Figure 1](image-url)  
*Flow diagram of experimental model. Each animal was initially ventilated while baseline data were 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 the simplified automatic ventilator (SAVe). On failure of the SAVe ventilator, or after a 1-hr period, they were ventilated with the Siemens Servo 900C. Comparisons of ventilator capability to support each pig were made at the end of each time period (large arrows).*

**RESULTS**

**SAVe I**

There was no difference in PaO₂ or PaO₂/FIO₂ ratio at baseline, whether ventilated by Servo or SAVe I (Table 2). However, PaCO₂ was lower while undergoing baseline ventilation with the SAVe I and Ve was greater. Lung compliance tended to be greater during baseline ventilation with the Servo, although 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 experienced 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 PaO₂/FIO₂ ratio ranging from 91 to 288 (median 129). Measured dead space fraction (measured while ventilated with the Siemens) increased from 0.49 ± 0.06 before injury to 0.68 ± 0.09 after injury (p = .003), whereas measured compliance decreased from 21.3 ± 9.0 mL/cmH₂O to 8.8 ± 1.9 mL/cmH₂O (p = .03) after lung injury.

The SAVe I ventilator was capable of supporting only one of the six animals after development of ALI. For the remaining five animals, the SAVe I was not capable of maintaining measured oxygen...
Table 2. Baseline measured physiologic parameters for ventilation with the SAVe I, SAVe II, or Siemens Servo 900C

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAVe I (n = 6)</th>
<th>SAVe II (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pao₂ (torr)</td>
<td>92.5 ± 9.1</td>
<td>92.5 ± 14.1</td>
</tr>
<tr>
<td>Paco₂ (torr)</td>
<td>37.7 ± 1.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>37.7 ± 4.2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Expired volume per min (L/min)</td>
<td>5.7 ± 1.5&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>8.3 ± 0.8&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>Peak airway pressure (cm H₂O)</td>
<td>16.7 ± 2.1</td>
<td>14.7 ± 3.4</td>
</tr>
<tr>
<td>Compliance (mL/cm H₂O)</td>
<td>21.3 ± 9.0</td>
<td>15.6 ± 5.2</td>
</tr>
<tr>
<td>Pao₂/Fio₂ ratio</td>
<td>440 ± 43</td>
<td>440 ± 67</td>
</tr>
<tr>
<td>Mean blood pressure (mm Hg)</td>
<td>106.5 ± 3.1</td>
<td>98.9 ± 13.9</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mm Hg)</td>
<td>17.5 ± 1.5</td>
<td>15.6 ± 2.6</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>2.47 ± 0.40</td>
<td>2.83 ± 0.60</td>
</tr>
<tr>
<td>Pulmonary artery occlusion pressure</td>
<td>7.63 ± 0.98&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.83 ± 0.98&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are mean ± sd. *p = .001; **p = .007; *p = .02; *p = .048; *p = .01. Comparisons are made between Siemens Servo and SAVe ventilators in each group. *p > .05 unless specified.

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAVe I</th>
<th>SAVe II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pao₂ (torr)</td>
<td>106.0 ± 26.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>52.0 ± 11.1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Paco₂ (torr)</td>
<td>57.8 ± 11.3</td>
<td>56.3 ± 19.7</td>
</tr>
<tr>
<td>Expired volume per min (L/min)</td>
<td>5.9 ± 2.0</td>
<td>5.5 ± 1.1</td>
</tr>
<tr>
<td>Compliance (mL/cm H₂O)</td>
<td>8.8 ± 1.9</td>
<td>5.9 ± 2.9</td>
</tr>
<tr>
<td>Pao₂/Fio₂ ratio</td>
<td>147.2 ± 71.1</td>
<td>93.2 ± 32.3</td>
</tr>
<tr>
<td>Mean blood pressure (mm Hg)</td>
<td>97.3 ± 18.4</td>
<td>106.7 ± 25.9</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mm Hg)</td>
<td>35.1 ± 9.1</td>
<td>46.7 ± 17.2</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>1.55 ± 0.53</td>
<td>1.71 ± 0.51</td>
</tr>
<tr>
<td>Pulmonary artery occlusion pressure (mm Hg)</td>
<td>12.50 ± 4.00</td>
<td>14.30 ± 6.06</td>
</tr>
<tr>
<td>Peak end-expiratory pressure (cm H₂O)</td>
<td>6.7 ± 3.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fio₂</td>
<td>0.80 ± 0.25</td>
<td>0.58 ± 0.06</td>
</tr>
<tr>
<td>Peak airway pressure (cm H₂O)</td>
<td>30.8 ± 7.2</td>
<td>29.5 ± 6.9</td>
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</table>

Values are mean ± sd. *p = .002; **p = .003. Comparisons are made between Siemens Servo and SAVe I ventilators. *p > .05 unless specified.

saturation >80% for at least 1 hr after completion of oleic acid infusion. In contrast, the Siemens Servo 900C was capable of maintaining specified clinical variables in all six animals. Pao₂ was lower while being ventilated with the SAVe I ventilator compared to the Servo (Table 3). The decrease in Pao₂ coincided with a lower Fio₂ and PEEP, although the difference in Fio₂ delivered was not statistically significant. There was no statistically significant difference in Pao₂/Fio₂ ratio, Paco₂, Ve, 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 Pao₂, Paco₂, Ve, or Pao₂/Fio₂ 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, whereas 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 Pao₂/Fio₂ 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 ± 0.04 before injury to 0.64 ± 0.13 after injury (p = .02), whereas measured compliance decreased from 27.8 ± 10.4 ml/cm H₂O to 10.4 ± 4.1 ml/cm H₂O (p = .008) after lung injury. The SAVe II ventilator was capable of supporting all six animals for at least 1 hr after development of ALI based on pre-specified clinical requirements using lung-protective ventilation and permissive hypercapnia. There was no statistically significant difference in measured Pao₂, Paco₂, Ve, compliance, Pao₂/Fio₂ ratio, PAOP, cardiac output, peak airway pressure, PEEP, Fio₂, 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, Pao₂/Fio₂ 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 ALI 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, whereas the additional features of the SAVe II allowed successful short-term ventilation and oxygenation despite severe lung injury. The failure of the SAVe I was likely attributable to ventilator limitations rather than extreme levels of respiratory failure, because 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 ALI obtained, by using a crossover design we were able to demonstrate that the SAVe I was not capable of supporting any level of lung injury for 1 hr, whereas the Servo was able to support a similar degree of lung injury. No significant difference in Pao₂/Fio₂ ratio was present in the animals at peak lung injury or respiratory failure when ventilated by the SAVe I ventilator or Servo; the nonsignificant difference that was observed likely reflects the difference in PEEP between the two groups more so than a difference in the severity of lung injury.

The respiratory alkalosis observed in the animals using the SAVe I ventilator before lung injury is a consequence of the
Table 4. Physiologic variables at failure of mechanical ventilation or peak lung injury while being supported with SAVe II or Siemens 900C (n = 6)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Servo</th>
<th>SAVe II</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Pao_2) (torr)</td>
<td>158.3 ± 167.7</td>
<td>141.8 ± 169.3</td>
</tr>
<tr>
<td>(Paco_2) (torr)</td>
<td>58.5 ± 17.0</td>
<td>52.5 ± 10.4</td>
</tr>
<tr>
<td>Expired volume per min (L/min)</td>
<td>5.2 ± 1.4</td>
<td>5.0 ± 1.3</td>
</tr>
<tr>
<td>Compliance (mL/cmH(_2)O)</td>
<td>10.4 ± 4.1</td>
<td>8.6 ± 3.8</td>
</tr>
<tr>
<td>(PaO_2/\text{FiO}_2) ratio</td>
<td>244.2 ± 140.8</td>
<td>224.8 ± 145.8</td>
</tr>
<tr>
<td>Mean blood pressure (mm Hg)</td>
<td>94.5 ± 22.5</td>
<td>90.8 ± 22.0</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mm Hg)</td>
<td>32.2 ± 5.4</td>
<td>32.7 ± 4.0</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>2.94 ± 0.72</td>
<td>2.03 ± 0.75</td>
</tr>
<tr>
<td>Pulmonary artery occlusion pressure (mm Hg)</td>
<td>10.58 ± 3.77</td>
<td>11.50 ± 4.85</td>
</tr>
<tr>
<td>Peak end-expiratory pressure (cm H(_2)O)</td>
<td>7.7 ± 2.6</td>
<td>5.7 ± 1.2</td>
</tr>
<tr>
<td>(FiO_2)</td>
<td>0.61 ± 0.30</td>
<td>0.58 ± 0.30</td>
</tr>
<tr>
<td>Peak airway pressure (cm H(_2)O)</td>
<td>31.7 ± 7.3</td>
<td>36.2 ± 10.8</td>
</tr>
</tbody>
</table>

Values are mean ± sd. Comparisons are made between Siemens Servo and SAVe II ventilators. \(p > .05\) for all comparisons.

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 \(Vr\) on a limited-function surge ventilator that should be capable of providing ventilation to patients with varying degrees of lung injury.

In this experiment, the Food and Drug Administration-approved SAVe I, a device with a compressor capable of flows of 16 L/min and with a fixed respiratory rate and \(Vr\), was unable to adequately oxygenate a porcine model of oleic acid-induced ALI. In contrast, the SAVe II ventilator, which incorporates a compressor capable of flow at 80 L/min, adjustable \(Vr\) and respiratory rate, and the ability to deliver \(FiO_2\) up to 1.0 and maintain PEEP, was able to oxygenate and ventilate the pigs for up to 1 hr. 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 1 hr. This difference is likely attributable to the ability of SAVe II to provide higher levels of \(FiO_2\) 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, in whom 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 been the case in clinical studies or recent experience (28). The majority of H5N1 patients with respiratory failure have ARDS (29, 30), as do patients with seasonal influenza (31) or H1N1 influenza (32–36). Hence, we believe that our model, which allows for titration of \(Pao_2/\text{FiO}_2\) 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 \(Pao_2/\text{FiO}_2\) < 100 in patients with respiratory failure attributable 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 less ill patients, patients improving, and patients ventilated for reasons other than pulmonary pathology (e.g., traumatic brain injury). Yet the ability of these devices to have some utility for the predominant cause of the mass respiratory failure remains a logical requirement for stockpiling.

Of note, whereas 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 require-

ments. Furthermore, 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. Although 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 ALI 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. Whereas some have offered the polio epidemic of the 1950s as evidence that patients with respiratory failure can be supported with limited supportive techniques, such patients experienced neuro muscular 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 (Richmond Agitation and Sedation Score < 5); therefore, they were not challenged with ventilator dysynchrony as commonly seen in humans with respiratory failure who retain a spontaneous ventilatory drive. This model is better equipped to assess the ability of the ventilators to support hypoxic respiratory failure than hypercapnic respiratory failure. Last, there was no noticeable air flow 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 before 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, air flow obstruction, and severely ill pediat-
ric 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, still be necessary to prove clinical utility for devices that passed initial screening tests.

CONCLUSION

We describe a novel in vitro 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, whereas the SAVe II ventilator is able to support a comparable level of hypoxemic respiratory failure secondary to ALI/ARDS for 1 hr. We recommend further study assessing longer duration and different etiologies and aspects of respiratory failure before large-scale procurement of these devices.

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