Pressure-Regulated Volume Control Ventilation vs Synchronized Intermittent Mandatory Ventilation for Very Low-Birth-Weight Infants

A Randomized Controlled Trial

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Objective: To test the hypothesis that pressure-regulated volume control (PRVC), an assist/control mode of ventilation, would increase the proportion of very low-birth-weight infants who were alive and extubated at 14 days of age compared with synchronized intermittent mandatory ventilation (SIMV).

Study Design: Ventilated infants with birth weight of 500 to 1249 g were randomized at less than 6 hours of age either to pressure-limited SIMV or to PRVC on the Servo 300 ventilator (Siemens Electromedical Group, Danvers, Mass). Infants received their assigned mode of ventilation until extubation, death, or meeting predetermined failure criteria.

Results: Mean ± SD birth weights were similar in the SIMV (888 ± 199 g, n = 108) and PRVC (884 ± 203 g, n = 104) groups. No differences were detected between SIMV and PRVC groups in the proportion of infants alive and extubated at 14 days (41% vs 37%, respectively), length of mechanical ventilation in survivors (median, 24 days vs 33 days, respectively), or the proportion of infants alive without a supplemental oxygen requirement at 36 weeks’ postmenstrual age (57% vs 63%, respectively). More infants receiving SIMV (33%) failed their assigned ventilator mode than did infants receiving PRVC (20%). Including failure as an adverse outcome did not alter the overall outcome (39% of infants in the SIMV group vs 35% of infants in the PRVC group were alive, extubated, and had not failed at 14 days).

Conclusion: In mechanically ventilated infants with birth weights of 500 to 1249 g, using PRVC ventilation from birth did not alter time to extubation.

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Lung injury following mechanical ventilation remains a significant cause of mortality and morbidity in premature infants who require respiratory support. Intermittent mandatory ventilation (IMV) using pressure-limited, time-cycled ventilators was, for many years, the only practical mode of mechanical ventilation for these infants. Advances in ventilator technology have made it possible to ventilate newborns using ventilator breaths synchronized to an infant’s spontaneous breaths and thereby to provide assist/control ventilation (ACV) in which the infant receives a full mechanical breath with each spontaneous breath. These newer modes may have the potential to limit ventilator-induced lung injury in newborn infants. Both synchronized IMV (SIMV) and ACV may reduce time on the ventilator for newborns as compared with nonsynchronized IMV.6,7 Although limited data suggest that ACV in newborn infants may improve physiological parameters and speed ventilator weaning as compared with SIMV,5 other longer-term effects of the 2 modes have not been compared in premature infants.

The objective of this study was to compare pulmonary outcomes in very low-birth-weight infants receiving ACV with those in infants receiving SIMV. We hypothesized that, among infants who weighed 500 to 1249 g at birth, pressure-regulated volume control ventilation (PRVC, a specific type of ACV) would increase the proportion of infants who were alive and extubated at 14 days of age compared with SIMV.

METHODS

PATIENT POPULATION

This study was conducted in 2 level III neonatal intensive care units. Infants with birth
weights of 500 to 1249 g and gestational ages of 24 weeks or older at birth who required mechanical ventilation were eligible for enrollment. Obstetrical dating was used to assign gestational age unless it was unavailable or varied from new Ballard examination by more than 2 weeks. In these cases, Ballard dating was used. Infants were enrolled before 6 hours of age, following informed consent. The University of Rochester and Vassar Brothers Medical Center institutional review boards approved this study.

VENTILATION MODES

All of the study subjects received mechanical ventilation using the Servo 300 ventilator (Siemens Electromedical Group, Danvers, Mass). Subjects were randomly assigned to 1 of 2 modes of ventilation. Subjects assigned to the SIMV group were placed on SIMV pressure control/pressure support, a synchronized, pressure-limited mode of IMV. Pressure support was set to 0 cm H2O (0 kPa) for subjects on this mode to maximize the difference in the number of supported breaths between SIMV and PRVC. The Servo 300 ventilator has a maximum SIMV rate of 40 breaths per minute. Infants receiving SIMV who required a higher ventilatory rate were changed to pressure-limited SIMV on the Bird VIP ventilator (Bird Products Corp, Palm Springs, Calif) until the rate fell to less than 40 breaths per minute. Subjects assigned to the PRVC group were placed on PRVC, a synchronized, pressure-limited assist/control mode that sequentially varies the delivered pressure to approximate a target inspiratory tidal volume. The modes of ventilation were not masked.

The Servo 300 ventilator measures flows and tidal volumes proximal to the inspiratory limb. The ventilator uses identical triggering, flow patterns, and breath termination parameters for both pressure-limited SIMV and PRVC. Breaths are flow triggered, with trigger levels ranging from 3 mL/s to 32 mL/s. In this study, the trigger level was set at the most sensitive level that did not result in automatic triggering. Breaths are terminated at a set proportion of the respiratory cycle that cannot exceed 80% of the cycle. Breaths are delivered using a decelerating flow pattern. In the modes used, the Servo 300 does not use flow termination of ventilator breaths.

RESPIRATORY MANAGEMENT

Target PaO2 values were 45 to 60 torr (6.0-8.0 kPa) for infants born at 24 to 26 weeks' gestation, 50 to 70 torr (6.7-9.3 kPa) for infants born at 27 to 28 weeks' gestation, and 60 to 80 torr (8.0-10.6 kPa) for infants born at more than 28 weeks' gestation. Target PaCO2 values were 45 to 55 torr (6.0-7.3 kPa) regardless of gestational age at birth. Specific ventilator settings to achieve these targets were determined by the clinical team. Infants continued to receive their randomized assigned mode of ventilation until they were extubated, died, or met the failure criteria.

Infants were considered to have “failed” their assigned mode of ventilation if they met any 1 of the following conditions:

1. PaO2 of less than 45 torr (6.0 kPa) for infants born at 26% or fewer weeks' gestation or PaO2 of less than 50 torr (6.7 kPa) for infants born at 27% or more weeks' gestation on 2 arterial blood gas determinations at least 2 hours apart, with the infant receiving a fraction of inspired oxygen concentration (FiO2) of 1.0 and a mean airway pressure of 9 cm H2O (0.9 kPa) or higher for infants who weighed less than 1000 g or 10 cm H2O (1.0 kPa) or higher for infants who weighed 1000 g or more at the time of failure.
2. PaCO2 of higher than 60 torr (8.0 kPa) on 2 blood gas determinations at least 4 hours apart, with the infant receiving a mean airway pressure of 9 cm H2O (0.9 kPa) or higher for infants who weighed less than 1000 g or 10 cm H2O (1.0 kPa) for infants who weighed 1000 g or more at the time of failure.
3. Pao2 of less than 30 torr (4.0 kPa) on 2 blood gas determinations over 4 hours, with the infant receiving a mean airway pressure of 4 cm H2O (0.4 kPa) or less in infants who still required mechanical ventilation owing to apnea or other reasons.
4. The attending neonatologist felt that it was detrimental to continue the assigned treatment.

If the infant met any of the failure criteria, the infant could be changed to any mode of ventilation, including the mode used for subjects in the other arm of the trial or high-frequency ventilation. Infants switched to other modes were returned to their assigned mode of ventilation as soon as the attending neonatologist felt that their clinical status permitted this.

A trial of extubation was required if an infant met all of the following criteria:

1. The FiO2 was 0.35 or less and was not increasing.
2. The mean airway pressure was 6 cm H2O (0.6 kPa) or less for infants with a current weight of less than 1000 g or 8 cm H2O (0.8 kPa) or less for infants with a current weight of 1000 g or more.
3. A current weight of 900 g or more in an infant who was at 80% of birth weight or greater.

Infants could also be extubated at any time prior to meeting mandatory extubation criteria if the attending neonatologist felt this was clinically indicated.

If the postmenstrual age (PMA) was less than 32 weeks at the time of attempted extubation, methylxanthine treatment was initiated prior to extubation. If the weight was less than 1000 g at the time of attempted extubation, the infant was extubated to nasal continuous positive airway pressure. Extubated infants were reintubated only if clinically indicated. Infants placed back on mechanical ventilation were placed back on their assigned mode of study ventilation. If an infant failed extubation, the extubation was reattempted within 7 days if the infant continued to meet the extubation criteria.

MEASUREMENTS

Respiratory physiological parameters were recorded at 6, 12, 24, 30, 48, and 72 hours of age, 14 and 28 days of age, and 36 weeks' PMA. Dynamic compliance was measured in mechanically ventilated infants at each time point using a Bicore pulmonary function monitor (SensorMedics, Irvine, Calif). Bronchopulmonary dysplasia was defined as continued requirement for supplemental oxygen and/or ventilatory support at 36 weeks' PMA. Age at final extubation was defined as the day on which a child was extubated and remained alive and extubated thereafter. For this calculation, children who died were defaulted to beyond the longest time of intubation.

Routine developmental follow-up was performed at 1 center for all infants with a birth weight of less than 1250 g. The evaluation at 6 to 9 months' corrected age included examination by a pediatric neurologist and the Bayley Scales of Infant Development Mental Developmental Index. Infants were reevaluated at 12 to 18 months of age if the initial evaluation produced abnormal or suspect findings. The results of the final evaluation were recorded.

STATISTICAL METHODS

Subjects were randomized using a block randomization scheme generated by random assortment by 1 of the investigators (R.M.R.). Block size (8 infants per block) was concealed from
those who were randomizing infants. Randomization was strati-

fied by birth weight (<1000 g and ≥1000 g) and center using

sealed, opaque envelopes.

The data were analyzed by intention to treat. The primary

outcome was the proportion of infants who were alive and ex-
tubated at 14 days of age. Differences between groups were ex-
pressed as mean (or median) differences and 95% confidence
intervals for continuous or ordinal variables and as relative

rates and 95% confidence intervals for categorical data. Confidence

intervals for median differences were obtained by bootstrap-

ping. Time-to-event data were presented as Kaplan-Meier curves.

RESULTS

Subjects were enrolled between February 4, 1998, and

October 21, 2002. One center enrolled 178 subjects and the other enrolled 35 subjects (Figure 1).

BASELINE CHARACTERISTICS

Demographic and baseline characteristics were similar

between groups (Table 1). All of the infants were born at

or before 32 weeks’ PMA. A high proportion of in-

fants in each study group was born to mothers who had

received antenatal glucocorticoids.

RESPIRATORY OUTCOMES

The ventilator settings and acute physiological measure-

ments at 6 hours of age (immediately following study en-

try) and 12 hours of age (6 hours after the switch to study

mode) are listed in Table 2. Subjects in the PRVC group

had higher ventilator rates but lower inspiratory tidal vol-

umes and peak inspiratory pressures than subjects in the

SIMV group. However, minute ventilation did not differ

between groups. At 12 hours of age among subjects who

had an arterial blood gas analysis performed, adherence

to PaO2 targets was good but PaCO2 was maintained lower

than the targeted range. Dynamic compliance (data not

shown) did not differ between groups at 6 or 12 hours.

The pattern of higher ventilator rates and lower tidal vol-

umes in the PRVC group persisted at 24, 48, and 72 hours

of age (data not shown), but these numbers became less

and less representative of the groups as infants were ex-
tubated, died, or failed their mode of ventilation. Only about

60% of either group (64 of 108 subjects in the SIMV group;

62 of 104 subjects in the PRVC group) remained on the

ventilator on the assigned mode at 72 hours, with about

30% in each group (31 of 108 subjects in the SIMV group;

31 of 104 subjects in the PRVC group) extubated.

The number of infants alive and extubated did not differ

between the groups at 14 days, 28 days, or 36 weeks’

PMA (Table 3). Similarly, the proportion of infants who

were alive without bronchopulmonary dysplasia at 36

weeks’ PMA did not differ between groups. The overall

proportion of deaths also did not differ between groups.

The majority of deaths occurred in the first 14 days. The

additional outcome of age at final extubation (Figure 2)

was also examined. Although more infants in the SIMV

group had reached final extubation by 14 days of age, the

median time to final extubation among survivors did not
differ significantly between groups (Table 3).

Infants assigned to the SIMV group were more likely

to fail their assigned mode of ventilation than were in-

fants in the PRVC group (Table 4). No infant failed his or

her assigned mode on the basis of hypocarbia. Of the 36

subjects in the SIMV group who failed their assigned

mode, 25 were switched to PRVC, 8 were switched to

high-frequency oscillatory ventilation, and 3 were

switched to other ventilator modes. Of the 21 subjects

in the PRVC group who failed their assigned mode, 1

continued to receive PRVC, 15 were switched to high-

frequency oscillatory ventilation, and 5 were switched to

other ventilator modes. Failure was also highly asso-

ciated with remaining intubated at 14 days (53 [92%] of

57 infants who failed), 28 days (48 [84%] of 57 infants

who failed), and 36 weeks’ PMA (25 [45%] of 56 infants

who failed), with bronchopulmonary dysplasia or death

at 36 weeks’ PMA (45 [80%] of 56 infants who failed)

and with death (20 [36%] of 56 infants who failed). Thus,

failure appeared to be a marker for more severe disease.

Nearly all of the infants who failed (excepting only 2 in-

fants per group) remained intubated at 14 days. Con-

trolling for study failure by including failure as an ad-

verse outcome, however, did not alter the results (Table 4).

OTHER OUTCOMES

There were no differences between groups with respect

to other measures of lung disease severity or outcomes of

prematurity (Table 5). Of the 134 subjects from 1

center who survived to discharge, 83% were seen in fol-
low-up. The subjects seen in follow-up were similar in demographic characteristics and primary respiratory outcome to surviving subjects from the same center who were not seen in follow-up, except white children were over-represented in the follow-up group (relative risk, 1.7; 95% confidence interval, 1.03-2.82). There were no differences in neurodevelopmental outcome between subjects in the 2 study groups (Table 6).

Protocol deviations were identified in 61 infants. Small numbers of infants were enrolled outside allowable birth weights (n = 2), gestational ages (n = 4), or postnatal ages (n = 3). The most common major deviation was brief alteration of ventilatory mode (n = 27). Infants were returned to their assigned ventilatory mode as soon as the deviation was discovered. All infants were analyzed regardless of protocol deviations.

<table>
<thead>
<tr>
<th>Table 1. Demographic and Baseline Characteristics</th>
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<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Birth weight, g</td>
</tr>
<tr>
<td>Gestational age, wk</td>
</tr>
<tr>
<td>Boys</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Maternal glucocorticoid treatment</td>
</tr>
<tr>
<td>Maternal preeclampsia</td>
</tr>
<tr>
<td>Maternal chorioamnionitis</td>
</tr>
<tr>
<td>Apgar score (5 min)</td>
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<tr>
<td>Surfactant given</td>
</tr>
<tr>
<td>Entry FIO2</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; FIO2, fraction of inspired oxygen; MD, mean or median difference, as appropriate; NA, not applicable; PRVC, pressure-regulated volume control; RR, relative risk (for proportions); SIMV, synchronized intermittent mandatory ventilation.

*All RR and MD values are reported as PRVC to SIMV.
†Value expressed as mean (SD).
‡Value expressed as number (percentage).
§Value expressed as median (range).

<table>
<thead>
<tr>
<th>Table 2. Ventilator Settings and Acute Physiological Measurements</th>
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<tbody>
<tr>
<td>SIMV*</td>
</tr>
<tr>
<td>At 6 h of age</td>
</tr>
<tr>
<td>On assigned mode</td>
</tr>
<tr>
<td>FiO2</td>
</tr>
<tr>
<td>Ventilator rate, breaths/min§</td>
</tr>
<tr>
<td>Peak inspiratory pressure, cm H2O</td>
</tr>
<tr>
<td>Mean airway pressure, cm H2O</td>
</tr>
<tr>
<td>Tidal volume, mL/kg¶</td>
</tr>
<tr>
<td>Minute ventilation, mL /kg·min−1</td>
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<tr>
<td>Paco2, torr</td>
</tr>
<tr>
<td>Oxygenation index</td>
</tr>
<tr>
<td>Arterial to alveolar O2 ratio</td>
</tr>
<tr>
<td>At 12 h of age</td>
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<tr>
<td>On assigned mode</td>
</tr>
<tr>
<td>FiO2</td>
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<td>Arterial to alveolar O2 ratio</td>
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</tbody>
</table>

Abbreviations: CI, confidence interval; FIO2, fraction of inspired oxygen; MD, mean difference; NA, not applicable; PRVC, pressure-regulated volume control; RR, relative risk; SIMV, synchronized intermittent mandatory ventilation.

*Values expressed as mean (SD) unless otherwise indicated.
†All RR and MD values are reported as PRVC to SIMV.
‡Value expressed as number (percentage).
§Ventilator rate calculated as ventilator breaths delivered (set rate for SIMV; set rate or spontaneous respiratory rate, whichever was greater, for PRVC).
‖Result is statistically significant.
¶Inspiratory tidal volume, measured at ventilator, without compensation for tubing.

SI conversion factors: 1 cm H2O = 0.098 kPa; 1 torr = 0.133 kPa.
Table 3. Respiratory Outcomes

<table>
<thead>
<tr>
<th></th>
<th>SIMV*</th>
<th>PRVC*</th>
<th>RR (95% CI)†</th>
<th>MD (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive and extubated at 14 days</td>
<td>44/108 (41)</td>
<td>38/104 (37)</td>
<td>0.90 (0.64-1.26)</td>
<td>NA</td>
</tr>
<tr>
<td>Alive and extubated at 28 days</td>
<td>55/106 (52)</td>
<td>47/104 (45)</td>
<td>0.87 (0.66-1.15)</td>
<td>NA</td>
</tr>
<tr>
<td>Alive and extubated at 36 weeks’ PMA</td>
<td>88/105 (84)</td>
<td>87/104 (84)</td>
<td>1.0 (0.89-1.12)</td>
<td>NA</td>
</tr>
<tr>
<td>Alive without BPD at 36 weeks’ PMA</td>
<td>60/105 (57)</td>
<td>66/104 (63)</td>
<td>1.1 (0.89-1.38)</td>
<td>NA</td>
</tr>
<tr>
<td>BPD in survivors at 36 weeks’ PMA</td>
<td>32/92 (35)</td>
<td>27/93 (29)</td>
<td>0.83 (0.55-1.27)</td>
<td>NA</td>
</tr>
<tr>
<td>Died before discharge</td>
<td>13/107 (12)</td>
<td>13/104 (13)</td>
<td>1.03 (0.50-2.11)</td>
<td>NA</td>
</tr>
<tr>
<td>Age at final extubation in survivors, d§</td>
<td>24 (9-154)</td>
<td>33 (9-138)</td>
<td>NA</td>
<td>9 (-2.6 to 20.6)</td>
</tr>
<tr>
<td>Final extubation by 14 days</td>
<td>36/108 (33)</td>
<td>20/104 (19)</td>
<td>0.58 (0.36-0.93)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: BPD, bronchopulmonary dysplasia; CI, confidence interval; MD, median difference; NA, not applicable; PMA, postmenstrual age; PRVC, pressure-regulated volume control. *Values are expressed as number (percentage) unless otherwise indicated. †RR and MD values are reported as PRVC to SIMV. Respiratory outcome data were unavailable on 2 subjects in the SIMV group at 28 days and 3 subjects in the SIMV group at 36 weeks’ PMA, and these infants are not included in the analysis at those times. ‡Among the infants who died, 8 subjects in the SIMV group and 7 subjects in the PRVC group had died by 14 days of age, 12 subjects in the SIMV group and 9 subjects in the PRVC group had died by 28 days of age, and 13 subjects in the SIMV group and 11 subjects in the PRVC group had died by 36 weeks’ PMA. §Final extubation indicates that infants were extubated and remained alive and extubated thereafter. Information available in 92 SIMV subjects and 91 PRVC subjects.

Figure 2. Cumulative percentages of infants achieving final extubation over time. Age at final extubation was defined as the day on which a child was extubated and remained alive and extubated thereafter. Children who died were defaulted to beyond the longest time of intubation. Infants with an unknown final extubation date (n=3) were censored at the time last known to be intubated. The rate at which surviving children reached final extubation did not differ between study groups (median difference, 9 days; 95% confidence interval, −2.6 to 20.6). SIMV indicates synchronized intermittent mandatory ventilation; PRVC, pressure-regulated volume control.

Respiratory failure is a common problem in premature newborns. The traditional approach to mechanical ventilation of infants with respiratory failure was to use time-cycled, pressure-limited IMV. Maneuvers designed to entrain an infant’s respiratory efforts to the fixed ventilator rate, resulting in synchronization of ventilation, were found to improve gas exchange. During the past 15 years, synchronizing devices have been developed for use in newborns. When compared with IMV for newborns at identical inspiratory pressures, SIMV was found to improve many short-term respiratory parameters. Patients breathing synchronously with the ventilator were also found to have less variation in cerebral blood flow and arterial blood pressure than infants breathing asynchronously. With the advent of effective synchronized mechanical ventilation of newborns, ACV (also known as patient-triggered ventilation) in which every breath initiated by the patient is a full, synchronized mechanical breath became possible. Compared with IMV, ACV was also found to improve short-term respiratory parameters without increasing the risk of hypocarbia.

Several early studies of SIMV and ACV also showed more rapid weaning from the ventilator when these modes were compared with IMV. However, several subsequent randomized trials comparing either SIMV or ACV with IMV have not substantiated this effect. Although improvements were found in some subgroups, these studies did not show an overall improvement in bronchopulmonary dysplasia (at either 28 days of age or 36 weeks’ PMA) or death in subjects treated with synchronized modes. A recent systematic review of available studies concluded that although synchronized modes on the studied ventilators shortened the duration of mechanical ventilation, they did not alter the incidence of chronic lung disease.

Few direct comparisons between ACV and SIMV have been published. When applied during ventilator weaning, ACV promotes lower oxygen consumption than SIMV. In a small study comparing ACV with SIMV during ventilator weaning in infants of less than 35 weeks’ gestation during the recovery phase of their disease, infants receiving ACV had faster weaning times than those receiving SIMV (median, 24 hours vs 50 hours, respectively), and fewer ACV infants failed to wean from the ventilator. Our data suggest, however, that any potential advantages of 1 form of ACV (ie, PRVC) as compared with SIMV in newborns do not translate into measurable differences in pulmonary outcome.

Any study of ventilatory mode is prone to certain inherent problems. It is extremely difficult to mask the mode of ventilation, and all studies to date, including our own, have not been masked. This leads to the possibility of bias in application of differing modes or manipulation of the
outcome. Earlier studies have noted unequal rates of abandonment of assigned mode.28 Our study also found that one mode (SIMV) was more likely to be abandoned than was the other (PRVC). In keeping with the findings of others,28 we found that subjects who failed their assigned mode were more likely to be seriously ill, regardless of their initially assigned mode. A high crossover rate from SIMV to PRVC could have biased the results toward null if PRVC had, in reality, been superior. However, controlling for subjects who switched modes by constructing a composite outcome that included failure of study mode and failure of extubation did not alter the finding of no difference in outcome between modes.

This study was also powered for a relatively large difference in primary outcome between groups (20% absolute difference), so it is possible that a smaller difference could have been missed. The study also had relatively low power to detect small differences in the potentially more clinically relevant finding of bronchopulmonary dysplasia. However, in light of the similar rates of pulmonary outcomes between groups, any differences would likely be so small as to be clinically insignificant.

Ventilator-specific characteristics can be important in determining the outcome of ventilator mode studies. This study focused only on 2 ventilation modes provided by

### Table 4. Failure of Ventilatory Mode

<table>
<thead>
<tr>
<th></th>
<th>SIMV (n = 108)</th>
<th>PRVC (n = 104)</th>
<th>RR (95% CI)*</th>
<th>MD (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failed assigned mode</td>
<td>36 (33)†</td>
<td>21 (20)†</td>
<td>0.61 (0.38-0.97)</td>
<td>NA</td>
</tr>
<tr>
<td>Physiologically defined respiratory failure</td>
<td>14 (13)†</td>
<td>8 (8)†</td>
<td>0.98 (0.50-1.93)</td>
<td>NA</td>
</tr>
<tr>
<td>Attending neonatologist’s discretion</td>
<td>22 (20)†</td>
<td>13 (13)†</td>
<td>1.31 (0.66-2.54)</td>
<td>NA</td>
</tr>
<tr>
<td>FiO₂ *0.67 (0.29)†</td>
<td>0.75 (0.28)†</td>
<td>NA</td>
<td>0.07 (−0.09 to 0.23)</td>
<td>NA</td>
</tr>
<tr>
<td>PaO₂</td>
<td>0.18 (0.05-0.65)§</td>
<td>0.14 (0.05-0.48)§</td>
<td>NA</td>
<td>−0.04 (−0.18 to 0.10)</td>
</tr>
<tr>
<td>PacO₂, torr</td>
<td>63 (14)†</td>
<td>61 (13)†</td>
<td>NA</td>
<td>−2 (−10 to 6)</td>
</tr>
<tr>
<td>Alive, extubated, and not failed at 14 days of age</td>
<td>42 (39)†</td>
<td>36 (35)†</td>
<td>0.89 (0.62-1.3)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; FiO₂, fraction of inspired oxygen; MD, mean or median difference, as appropriate; NA, not applicable; PRVC, pressure-regulated volume control; RR, relative risk; SIMV, synchronized intermittent mandatory ventilation.

SI conversion factor: 1 torr = 0.133 kPa.

*All RR and MD values are reported as PRVC to SIMV.
†Value is expressed as number (percentage).
‡Value is expressed as mean (SD).
§Value is expressed as median (range).

### Table 5. Other Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SIMV*</th>
<th>PRVC*</th>
<th>RR (95% CI)†</th>
<th>MD (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary interstitial emphysema</td>
<td>5/108 (5)</td>
<td>8/104 (8)</td>
<td>1.7 (0.56-4.91)</td>
<td>NA</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>9/108 (8)</td>
<td>6/104 (6)</td>
<td>0.69 (0.26-1.87)</td>
<td>NA</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>3/108 (3)</td>
<td>3/104 (3)</td>
<td>1.04 (0.21-5.03)</td>
<td>NA</td>
</tr>
<tr>
<td>Systemic glucocorticoid therapy for BPD‡</td>
<td>42/104 (40)</td>
<td>37/99 (37)</td>
<td>0.93 (0.65-1.31)</td>
<td>NA</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>43/108 (40)</td>
<td>44/104 (42)</td>
<td>1.06 (0.77-1.47)</td>
<td>NA</td>
</tr>
<tr>
<td>Intraventricular hemorrhage &gt;= grade 3§</td>
<td>12/102 (12)</td>
<td>8/101 (8)</td>
<td>0.67 (0.29-1.58)</td>
<td>NA</td>
</tr>
<tr>
<td>Periventricular leukomalacia†</td>
<td>4/66 (5)</td>
<td>2/67 (2)</td>
<td>0.49 (0.09-2.63)</td>
<td>NA</td>
</tr>
<tr>
<td>To regain birth weight, d‡</td>
<td>11 (7)‖</td>
<td>12 (6)‖</td>
<td>NA</td>
<td>0.3 (−1.6 to 2.1)</td>
</tr>
<tr>
<td>Necrotizing enterocolitis requiring surgery†</td>
<td>3/105 (3)</td>
<td>4/100 (4)</td>
<td>1.4 (0.32-6.10)</td>
<td>NA</td>
</tr>
<tr>
<td>Threshold retinopathy of prematurity‡¶</td>
<td>8/76 (11)</td>
<td>6/77 (8)</td>
<td>0.74 (0.27-2.03)</td>
<td>NA</td>
</tr>
<tr>
<td>Home oxygen in survivors</td>
<td>7/94 (7)</td>
<td>5/91 (5)</td>
<td>0.74 (0.24-2.24)</td>
<td>NA</td>
</tr>
<tr>
<td>Days to discharge home in survivors</td>
<td>83 (30-195)#</td>
<td>87 (36-201)#</td>
<td>NA</td>
<td>4 (−4.4 to 12.4)</td>
</tr>
</tbody>
</table>

Abbreviations: BPD, bronchopulmonary dysplasia; CI, confidence interval; MD, mean or median difference, as appropriate; NA, not applicable; PRVC, pressure-regulated volume control; RR, relative risk; SIMV, synchronized intermittent mandatory ventilation.

*Values expressed as number (percentage) unless otherwise indicated.
†All RR and MD values are reported as PRVC to SIMV.
‡Subjects who did not have final information recorded for these variables are not included in these analyses.
§Classified according to Papile et al.10
‖Value is expressed as mean (SD).
¶At least 1 eye meeting Cryotherapy for Retinopathy of Prematurity criteria for surgery.11
#Value is expressed as median (range).
1 model of ventilator. The 2 strategies of ventilation produced differing patterns of ventilation in the infants, with ACV resulting in higher ventilator rates and lower tidal volumes than SIMV. Despite the differing strategies, no difference was found in outcome between the groups.

It is possible that using another ventilator model or mode could yield different effects. Triggering mechanisms continue to evolve, and more sensitive and specific systems may allow for better coordination of ventilator breaths with infant breaths.20–33 Although PRVC, which varies peak inspiratory pressures to achieve target tidal volumes, did not appear to make a difference in long-term outcomes in this study, other modes that target tidal volumes may show promise. “Volume guarantee” ventilation (Drager Medical, Lubeck, Germany) results in lower breath-to-breath tidal volume variability than non-volume-targeted modes while maintaining similar arterial blood gas values.35 In a recent trial,36 volume guarantee ventilation resulted in lower tracheal aspirate proinflammatory cytokine levels and faster ventilator weaning than a non-volume-targeted mode on the same simulator ventilation resulted in lower tracheal aspirate proinflammatory cytokine levels and faster ventilator weaning than a non-volume-targeted mode on the same.

Another recent study,37 however, did not support this finding. Other modes, such as “proportional assistance ventilation,” that seek to marry ventilator effort directly to the additional assistance a patient needs with each individual breath may also be useful.38,39

In summary, we have shown that when applied using the management approach specified in this trial, PRVC does not provide any measurable advantage over SIMV in the treatment of premature newborns with respiratory distress syndrome who have received surfactant therapy. It is important to continue to evaluate new concepts in conventional ventilation in prospective, randomized trials to optimize outcomes in premature infants.

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Additional Information: Dr D’Angio had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 6. Neurodevelopmental Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SIMV (n = 64)</th>
<th>PRVC (n = 64)</th>
<th>RR (95% CI)*</th>
<th>MD (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronological age at final eval.</td>
<td>13.1 (4.2)†</td>
<td>14.3 (3.7)†</td>
<td>NA</td>
<td>1.1 (−0.3 to 2.5)</td>
</tr>
<tr>
<td>Bayley MDI</td>
<td>90 (9)†</td>
<td>88 (12)†</td>
<td>NA</td>
<td>−2 (−5 to 2)</td>
</tr>
<tr>
<td>Abnormal neurologic evaluation</td>
<td>11 (17)‡</td>
<td>11 (17)‡</td>
<td>1.0 (0.47–2.14)</td>
<td>NA</td>
</tr>
<tr>
<td>Gross motor delay</td>
<td>11 (17)‡</td>
<td>11 (17)‡</td>
<td>1.0 (0.47–2.14)</td>
<td>NA</td>
</tr>
<tr>
<td>Fine motor delay</td>
<td>11 (17)‡</td>
<td>9 (14)‡</td>
<td>0.82 (0.36–1.84)</td>
<td>NA</td>
</tr>
<tr>
<td>Any abnormality§</td>
<td>12 (19)‡</td>
<td>13 (21)‡</td>
<td>1.08 (0.54–2.19)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MD, mean difference; MDI, Mental Developmental Index; NA, not applicable; PRVC, pressure-regulated volume control; RR, relative risk; SIMV, synchronized intermittent mandatory ventilation.

14. Bernstein G, Heldt GP, Mannino FL. Increased and more consistent tidal vol-
umes during synchronized intermittent mandatory ventilation in newborn infants. 

Am J Respir Crit Care Med. 1994;150:1444-1446.


