

# Adaptive Support Ventilation May Deliver Unwanted Respiratory Rate–Tidal Volume Combinations in Patients with Acute Lung Injury Ventilated According to an Open Lung Concept

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## ABSTRACT

**Background:** With adaptive support ventilation, respiratory rate and tidal volume ( $V_T$ ) are a function of the Otis least work of breathing formula. We hypothesized that adaptive support ventilation in an open lung ventilator strategy would deliver higher  $V_T$ s to patients with acute lung injury.

**Methods:** Patients with acute lung injury were ventilated according to a local guideline advising the use of lower  $V_T$  (6–8 ml/kg predicted body weight), high concentrations of positive end-expiratory pressure, and recruitment maneuvers. Ventilation parameters were recorded when the ventilator was switched to adaptive support ventilation, and after recruitment maneuvers. If  $V_T$  increased more than 8 ml/kg predicted body weight, airway pressure was limited to correct for the rise of  $V_T$ .

**Results:** Ten patients with a mean ( $\pm$ SD)  $\text{PaO}_2/\text{FiO}_2$  of  $171 \pm 86$  mmHg were included. After a switch from pressure-controlled ventilation to adaptive support ventilation, respiratory rate declined (from  $31 \pm 5$  to  $21 \pm 6$  breaths/min; difference = 10 breaths/min, 95% CI 3–17 breaths/min,  $P = 0.008$ ) and  $V_T$  increased (from  $6.5 \pm 0.8$  to  $9.0 \pm 1.6$  ml/kg predicted body weight; difference = 2.5 ml, 95% CI 0.4–4.6 ml/kg predicted body weight,  $P = 0.02$ ). Pressure limitation corrected for the rise of  $V_T$ , but minute ven-

## What We Already Know about This Topic

- Pressure-controlled ventilation (PCV) in patients with acute lung injury (ALI) allows protection against volutrauma

## What This Article Tells Us That Is New

- Switching from PCV to adaptive support ventilation in consecutive ALI patients led to decreased respiratory rates and increased tidal volumes in patients with more compliant lungs

tilation declined, forcing the user to switch back to pressure-controlled ventilation.

**Conclusions:** Adaptive support ventilation, compared with pressure-controlled ventilation in an open lung strategy setting, delivers a lower respiratory rate–higher  $V_T$  combination. Pressure limitation does correct for the rise of  $V_T$ , but leads to a decline in minute ventilation.

ADAPTIVE support ventilation (ASV), a microprocessor-controlled closed-loop mode of mechanical ventilation, provides automatic selection and continuous breath-by-breath adaptation of respiratory rate (RR) and tidal volume ( $V_T$ ).<sup>1,2</sup> With ASV clinicians can set neither RR nor  $V_T$  because the delivered RR- $V_T$  combination is a function of the Otis least work of breathing formula.<sup>3</sup>

Patients with acute lung injury (ALI) may benefit from measures that prevent repeated collapse and reexpansion of alveoli (*i.e.*, mechanical ventilation according to the “open lung concept”), including the use of higher concentrations of positive end-expiratory pressure (PEEP) and recruitment maneuvers (RMs).<sup>4</sup> Meta-analysis suggests this approach to prevent the need for rescue therapies for life-threatening hypoxemia,<sup>5</sup> and to prevent death of patients with more severe ALI.<sup>6</sup>

The use of higher concentrations of PEEP and RMs could make injured lungs more compliant.<sup>7,8</sup> This change in compliance could cause ASV to alter delivered RR- $V_T$  combinations. The Otis formula determines the RR that minimizes work of breathing for a clinician-set minute ventilation based on the expiratory time constant ( $\text{RC}_{\text{exp}}$ ) of the respiratory system. As  $\text{RC}_{\text{exp}}$  is obtained from the expiratory flow–volume curve, delivered RR- $V_T$  combinations should change with alterations of compliance of the respiratory system.<sup>9</sup> In

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the current study we determined RR-VT combinations with ASV in patients with ALI ventilated according to a local mechanical ventilation guideline using higher concentrations of PEEP and RMs.<sup>10</sup>

## Materials and Methods

### Patients and Informed Consent

Consecutive patients with ALI were included. The local medical ethical committee of our institute (Academic Medical Center, Amsterdam, The Netherlands) approved the study protocol and waived the need for informed consent because the objective of this study was to evaluate normal patient care.

### Study Design

This is a prospective observational study of patients observed during a change in the mechanical ventilation mode, from pressure-controlled ventilation to ASV.

### Inclusion Criteria

Patients were eligible for this study if they met the consensus criteria for ALI.<sup>11</sup> Only passive patients (*i.e.*, those who did not trigger the ventilator) who were considered hemodynamically stable (*i.e.*, could safely be subjected to RMs) were included. The ability to withstand RMs was judged by the clinician responsible for the patient.

### Mechanical Ventilation Protocols and RM

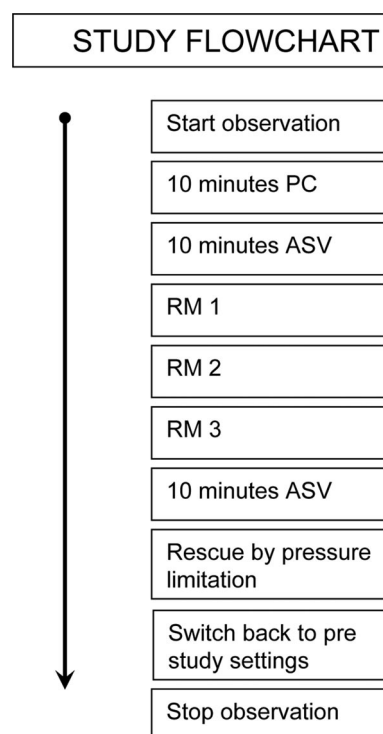
Patients were observed during mechanical ventilation when the ventilator was switched from pressure-controlled ventilation to ASV, and after additional RMs (fig. 1).

Patients underwent mechanical ventilation with a Hamilton Galileo ventilator (software version GMP03.41f, GCP03.40a, GTP01.00; Hamilton Medical AG, Rhäzüns, Switzerland). Passive humidification of the ventilatory circuit was applied with an HME filter (Medisize Hygrovent S, Medisize, Hillegom, The Netherlands).

Predicted body weight (PBW) was calculated using the following formula: in men,  $PBW\ (kg) = 50 + 0.91 \times (\text{centimeters of height} - 152.4)$ ; in women,  $PBW\ (kg) = 45.5 + 0.91 \times (\text{centimeters of height} - 152.4)$ .<sup>12</sup>

**Pressure-Controlled Ventilation.** A  $V_T$  of 6 ml/kg PBW as part of lung-protective ventilation was used. RR was set to maintain minute volume, ensuring a normal pH. The concentration of PEEP and  $F_{IO_2}$  was set, ensuring  $SpO_2$  of more than 90% and/or  $P_{aCO_2}$  of more than 10 kPa. As part of lung-protective ventilation, RMs were frequently performed before every increase of the PEEP concentration, and after every disconnection from the ventilator or suctioning.

**ASV.** The PBW was used to set body weight with ASV. PEEP and  $F_{IO_2}$  were kept the same as was pressure-controlled ventilation. Target minute ventilation was set at the percentage leading to the same minute ventilation as pressure-controlled mechanical ventilation. The initial airway pressure was set at



**Fig. 1.** Study flowchart showing the observed steps during the study with the duration of these steps. ASV = adaptive support ventilation; PC = pressure-controlled ventilation; RM = recruitment maneuver.

60 cm  $H_2O$  to allow ASV to reach the target minute ventilation. According to the software this initial pressure will lead to maximum plateau pressures of 50 cm  $H_2O$ .

**RMs.** In this study, we performed RMs to be certain that the lungs of studied patients were maximally recruited during the observations. RMs were performed as previously described.<sup>7</sup> The ventilator was set back to pressure-controlled ventilation and adjusted to deliver a sustained inflation, with an inflation pressure of 40 cm  $H_2O$  for 30 s.  $SpO_2$  and arterial blood pressure were monitored continuously during and after each RM. The effect was determined by a rise of the  $SpO_2$ . If the first RM was unsuccessful, a second RM was performed with an inflation pressure of 50 cm  $H_2O$  for 30 s. Eventually, a third RM was performed with an inflation pressure of 55 cm  $H_2O$  for 30 s.

**Rescue by Pressure Limitation.** In case  $V_T$  was more than 8 ml/kg PBW with ASV, the pressure limit alarm was decreased to the original pressure-controlled plateau pressure plus 10 cm  $H_2O$ , creating a target plateau pressure that was similar to the plateau pressure applied with pressure-controlled ventilation. However, when minute ventilation declined more than 20% below the target minute ventilation, the ventilator was switched back to pressure-controlled ventilation.

### Study Endpoint

The study endpoint was the change in RR- $V_T$  combinations before and after the switch of the ventilator from pressure-

controlled ventilation to ASV, the change in RR- $V_T$  combinations after additional RMs, and the change in RR- $V_T$  combinations after pressure limitation (if necessary). A change was defined as an increase or decrease of RR and  $V_T$  of 10% or greater.

### Data Collection

The following baseline data were collected: sex, body weight, height, cause of ALI/acute respiratory distress syndrome (ARDS), APACHE II score, duration of mechanical ventilation, length of stay in the intensive care unit, and mortality. The lung injury score was calculated.<sup>13</sup> Delivered RR- $V_T$  combinations were collected with a data logger connected to the ventilator (Hamilton Datalogger, version 3.27.1, Hamilton Medical AG, Rhäzüns, Switzerland). Blood gas parameters were collected from the Patient Data Management System (iMDsoft, Sassenheim, The Netherlands).

### Statistical Analysis

Data are presented as the mean with SD or medians with interquartile range where appropriate. Baseline data were analyzed with descriptive statistics. A general linear model for repeated measures (repeated measures ANOVA) was conducted to assess the difference in  $V_T$  between pressure-controlled ventilation, ASV before and after RMs, and after switching back to pressure-controlled ventilation. We performed an overall test; if significant differences were found we performed *post hoc* testing. To control for family-wise error we used protected testing for the follow-up *post hoc* tests. Bonferroni correction was used. Because the assumption of sphericity was violated, degrees of freedom were corrected using Greenhouse Geiser estimates of sphericity. Statistical significance was defined as a two-tailed *P* value < 0.05. All statistical analyses were performed in SPSS 16.0 (SPSS Inc., Chicago, IL).

## Results

### Patients

Ten consecutive patients with ALI who had been intubated and mechanically ventilated were included in the study. All patients were switched from pressure-controlled ventilation to ASV within 72 h after initiation of mechanical ventilation. Baseline characteristics are shown in table 1.

### Changes in RR- $V_T$ Combinations

After a switch from pressure-controlled ventilation to ASV, RR declined (from  $31 \pm 5$  to  $21 \pm 6$  breaths/min; difference = 10 breaths/min, 95% CI 3–17 breaths/min, *P* = 0.008) and  $V_T$  increased (from  $6.5 \pm 0.8$  to  $9.0 \pm 1.6$  ml/kg PBW; difference = 2.5 ml, 95% CI 0.4–4.6 ml/kg PBW, *P* = 0.02).

Although RR- $V_T$  combinations changed in seven patients, no changes were seen in three patients after switching the ventilator from pressure-controlled ventilation to ASV

**Table 1.** Clinical Characteristics of the Patients

Sex: male/female (n)	6/4
Age (yr, mean $\pm$ SD)	58 $\pm$ 23
Height (cm, mean $\pm$ SD)	173 $\pm$ 8
Actual body weight (kg, mean $\pm$ SD)	81 $\pm$ 16
Predicted body weight (kg, mean $\pm$ SD)	69 $\pm$ 9
Cause of ALI (n)	
Aspiration	1
Pneumonia	2
Sepsis	4
Other extrapulmonary causes	3
APACHE II score (mean $\pm$ SD)	28 $\pm$ 7
LIS (mean $\pm$ SD)	2.8 $\pm$ 0.5
Duration of mechanical ventilation (hours, median, IQR)	80 (53–143)
Dynamic compliance (ml/cm H <sub>2</sub> O)	37.2 $\pm$ 17.3
Pao <sub>2</sub> /Fio <sub>2</sub> (mmHg, mean $\pm$ SD)	171 $\pm$ 86
Fio <sub>2</sub>	0.5 $\pm$ 0.0
PEEP	10.9 $\pm$ 1.2

ALI = acute lung injury; APACHE II = Acute Physiology And Chronic Health Evaluation; Fio<sub>2</sub> = fraction of inspired oxygen; IQR = interquartile range; LIS = Lung Injury Score; Pao<sub>2</sub> = partial pressure of arterial oxygen; PEEP = positive end-expiratory pressure.

(fig. 2). Compared with patients in whom the switch from pressure-controlled ventilation to ASV resulted in a change in delivered RR- $V_T$  combinations, these patients had a higher lung injury score ( $3.3 \pm 0.3$  vs.  $2.7 \pm 0.2$ , *P* = 0.037), a decreased pulmonary compliance ( $23 \pm 5$  vs.  $44 \pm 17$  ml/cm H<sub>2</sub>O, *P* = 0.015), and a decreased RCexp ( $0.48 \pm 0.08$  vs.  $0.68 \pm 0.24$ , *P* < 0.001). There were no differences in causes of ALI between patients who showed a change in delivered RR- $V_T$  combinations after switching from pressure-controlled ventilation to ASV and those who did not.

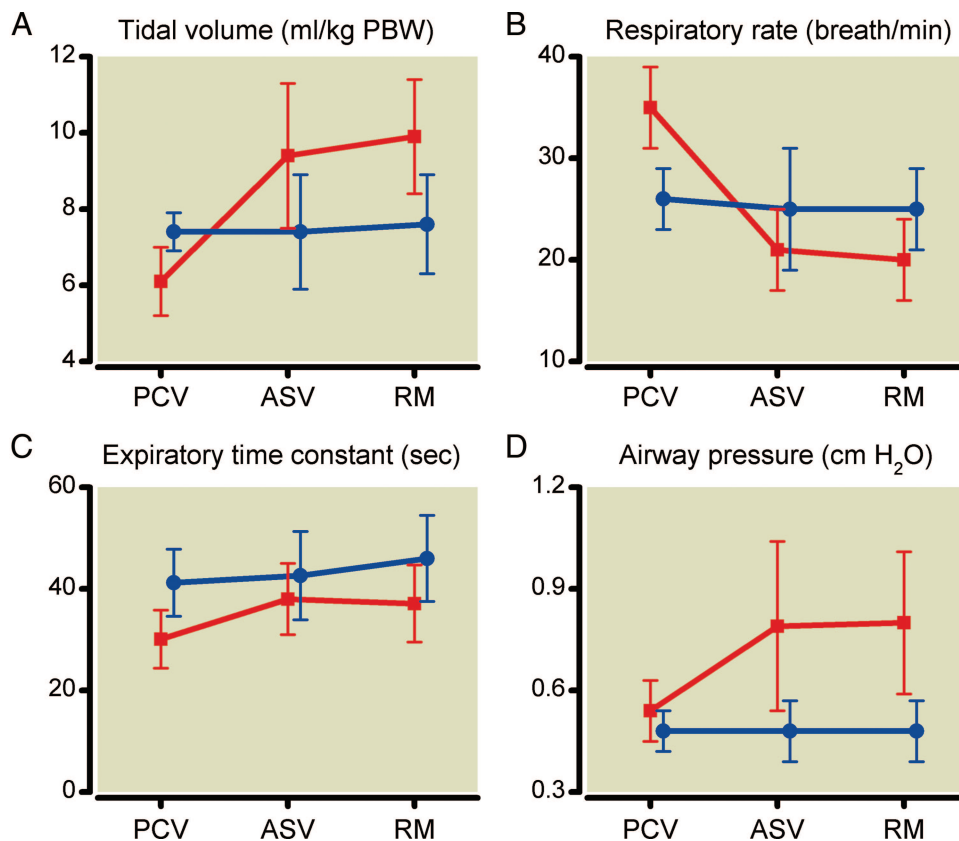
Nine patients were subjected to two RMs, and one patient to three RMs. In three patients the RM was stopped prematurely because of a decrease in systemic blood pressure. None of the nine patients responded to RMs with an increase in Spo<sub>2</sub> and/or PaCO<sub>2</sub>, suggesting that all recruitable lung parts were already recruited before switching from pressure-controlled ventilation to ASV. Differences in RR- $V_T$  combination with ASV before and after RMs were not statistically significant.

### Changes in Plateau Pressures

Plateau pressures increased when the ventilator was switched from pressure-controlled ventilation to ASV (from  $35 \pm 8$  to  $41 \pm 9$  cm H<sub>2</sub>O; difference = 6 cm H<sub>2</sub>O, 95% CI 3–8 cm H<sub>2</sub>O, *P* < 0.001). Differences in plateau pressures with ASV before and after RMs were not statistically significant.

### Rescue by Pressure Limitation

In seven patients in whom  $V_T$  was increased more than 8 ml/kg PBW after switching to ASV, the ventilation mode had to be switched back to pressure-controlled ventilation because minute ventilation decreased to unwanted low concentrations with



**Fig. 2.** Respiratory variables with pressure controlled ventilation (PCV), adaptive support ventilation (ASV), before and after recruitment maneuvers (RMs). Filled squares = seven patients with a change in delivered RR- $V_T$  combination after switch to ASV; filled circles = three patients without a change in delivered RR- $V_T$  combination after switch to ASV. Data are presented as mean  $\pm$  SD; PBW = predicted body weight.

pressure limitation (from  $13 \pm 2$  to  $8 \pm 1$  l/min; difference = 5 l/min, 95% CI  $-6$  to  $-3$  l/min,  $P < 0.001$ ).

### Changes After a Switch Back to Prestudy Ventilator Settings

At the end of the study, after switching back to pressure-controlled ventilation, differences in prestudy RR- $V_T$  combinations were not statistically significant (RR,  $31 \pm 6$  vs.  $32 \pm 7$  breaths/min; difference = 1 breaths/min, 95% CI  $-1$ – $4$  breath/min,  $P = 0.33$ ;  $V_T$   $6.4 \pm 0.8$  vs.  $6.5 \pm 0.9$  ml/kg PBW; difference = 0.1 ml/kg PBW, 95% CI  $-0.4$ – $0.7$ ,  $P = 0.56$ ).

### Discussion

The results of this observational study can be summarized as follows. (1) RR decreases and  $V_T$  increases when switching from pressure-controlled ventilation to ASV in patients with ALI ventilated according to an open lung concept; (2) in patients with less compliant (*i.e.*, more injured) lungs, ASV maintains  $V_T \leq 8$  ml/kg PBW; (3) in patients with more compliant (*i.e.*, less injured) lungs, ASV delivers  $V_T$  more than 8 ml/kg PBW; (4) pressure limitation on ASV can correct for this change, but leads to an unacceptable decrease of minute ventilation.

Our study has several limitations. First, it must be noted that the sample size of our study is small. Nevertheless, the observed changes are significant and consistent. Second, patients were not randomly assigned to an ASV and a control group; they served as their own control group. Furthermore, patients were recruited in one center, where a mechanical ventilation guideline with strict recommendations on higher concentrations of PEEP and RMs was being applied. This may not be the case in other centers and could have led to significantly different results. Another limitation is that we compared RR and  $V_T$  over time. One could postulate that over time, differences in compliance make comparison of RR- $V_T$  impossible. It should be noted, however, that collection of data was always within a short time span (30 min). Comparison of pressure-controlled ventilation with ASV may be a limitation. Volume-controlled ventilation was used in the ARDS Network trial,<sup>14</sup> and is recommended by the National Institutes of Health. However, we explicitly chose to observe changes from pressure-controlled ventilation to ASV, and *vice versa*, because ASV is a pressure-controlled mode of mechanical ventilation. In addition, because the subgroup analyses were conducted in response to review of the data, comparisons of this type tend to replicate less often than desired. It should be recognized that the researchers were not blinded for the ventilation mode.



Patients with ALI undoubtedly benefit from lung-protective mechanical ventilation using decreased  $V_T$ .<sup>14,15</sup> Therefore, current guidelines recommend using a  $V_T$  of 6–8 ml/kg in patients with ALI.<sup>10</sup> A subsequent analysis of the landmark study by the ARDS Network showed the beneficial effect of  $V_T$  reduction to be independent of the severity of ALI.<sup>16</sup> Patients with less severe ALI also benefited from lung-protective mechanical ventilation using decreased  $V_T$ . In light of these findings it seems imperative to use a  $V_T$  close to 6 ml/kg PBW in all patients with ALI. Our findings suggest that ASV is capable of keeping  $V_T$  within the desired range of protective ventilation, but only when lungs are severely injured. Our data show that ASV applies larger  $V_T$  when lungs are subjected to higher concentrations of PEEP and RMs.

One of the components of the ARDS Network's decreased  $V_T$  strategy was to also limit end-inspiratory stretching pressures (*i.e.*, plateau pressures) to less than 30 cm H<sub>2</sub>O, and to lower  $V_T$  to 4 ml/kg PBW if necessary.<sup>14</sup> In the current study maximum airway pressures with pressure-controlled ventilation were more than 30 cm H<sub>2</sub>O; maximum airway pressures were even higher with ASV. However, the concentrations of PEEP used in our study were higher than those used in the ARDS Network trial.<sup>14</sup> In addition,  $V_T$  was decreased to 4 ml/kg PBW with neither pressure-controlled ventilation nor ASV; with ASV, there was an increase in  $V_T$ , despite the high maximum airway pressures.

Results from two recent investigations, which evaluated ASV as a mechanical ventilation strategy in ALI/ARDS, seem to be in contrast with our findings. Sulemanji *et al.* studied the performance of ASV in a simulated lung injury model and compared the ability of ASV to maintain plateau pressure below a set target (28 cm H<sub>2</sub>O) in comparison with a fixed  $V_T$  of 6 ml/kg during controlled mechanical ventilation.<sup>17</sup> It should be noted that minute ventilation was sacrificed when RR and  $V_T$  reached predefined limits. This scenario may be impossible in the clinical setting. We chose not to sacrifice minute ventilation, resulting in unwanted RR- $V_T$  combinations. Arnal *et al.* studied delivered RR- $V_T$  combinations in a large group of intubated and mechanically ventilated patients.<sup>18</sup> They elegantly showed that ASV delivered decreased  $V_T$  in clinical conditions associated with shorter RCexp (*i.e.*, patients suffering from ALI). In that study, RCexp in patients with ALI were comparable to RCexp in the current study (0.51 s *vs.* 0.48–0.68 s). Arnal *et al.* did not report on the relation between RCexp and the size of  $V_T$  applied by ASV, although the report showed that ASV must have applied high  $V_T$  in certain cases. This is in line with our findings.

The results of our current study are in line with a recently published simulation study.<sup>19</sup> In a bench-to-bedside study we recently showed that ASV delivers high RR and low VT in a setting mimicking ALI. When the compliance of the test lung increased, RR decreased and VT increased. Delivered VT were more than 8 ml/kg PBW when compliance of the

test lung was set at concentrations that are achieved when using the open lung concept for ALI.

It is well known that the compliance of injured lungs increases when higher concentrations of PEEP and/or RMs are applied.<sup>7,8</sup> Lung compliances as high as 50 ml/cm H<sub>2</sub>O are reported in patients with ALI, when the open lung concept is applied.<sup>7</sup> It is also known that the compliance of injured lungs increases when lung injury resolves. Although our study did not investigate RR- $V_T$  combinations in the setting of resolving lung injury, our current data as well as results from our previous preclinical investigation<sup>19</sup> suggest that ASV may also apply  $V_T$  more than 8 ml/kg PBW in that situation. It is unknown whether this is unwanted in patients with resolving ALI. One could speculate that a minimal work strategy with larger  $V_T$ s and slower rates might produce less lung injury than a fixed 6–8 ml/kg  $V_T$  strategy. This strategy has not yet been tested in randomized controlled trials.

In conclusion, we found ASV to deliver possible unsafe RR- $V_T$  combinations in patients with ALI ventilated according to an open lung concept. Pressure limitation did correct for the unwanted increase of  $V_T$ , but it led to an unwanted decline in minute ventilation.

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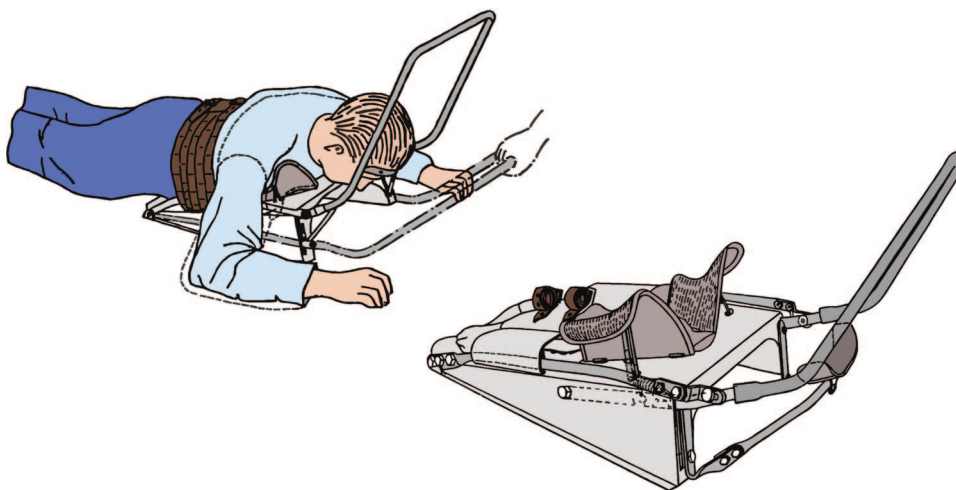
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## ANESTHESIOLOGY REFLECTIONS

### The Panis Apparatus: An Exercise in Artificial Respiration



In June of 1924, Germain Panis of France filed a U.S. Patent on an "Apparatus for Producing Artificial Respiration." According to the inventor, his device "enables the so-called Schaeffer [sic] method of artificial respiration to be . . . continued for a comparatively long time. . . ." (The original "hands-on" Schäfer method positioned the rescuer's knees alongside the prone victim's hips as the rescuer's hands rhythmically compressed the victim's lower ribs while rocking back and forth.) Ironically, any patient successfully resuscitated by the Panis Apparatus who lived to old age might enjoy choosing from a wide array of modern exercise machines which cite Panis' invention in their patent applications. (Copyright © the American Society of Anesthesiologists, Inc. This image also appears in the *Anesthesiology Reflections* online collection available at [www.anesthesiology.org](http://www.anesthesiology.org).)

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