Adaptive Support Ventilation for Fast Tracheal Extubation after Cardiac Surgery

A Randomized Controlled Study

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Background: Adaptive support ventilation (ASV) is a microprocessor-controlled mode of mechanical ventilation that maintains a predefined minute ventilation with an optimal breathing pattern (tidal volume and rate) by automatically adapting inspiratory pressure and ventilator rate to changes in the patient's condition. The aim of the current study was to test the hypothesis that a protocol of respiratory weaning based on ASV could reduce the duration of tracheal intubation after uncomplicated cardiac surgery (“fast-track” surgery).

Methods: A group of patients being given ASV (group ASV) was compared with a control group (group control) in a randomized controlled study. After coronary artery bypass grafting during general anesthesia with midazolam and fentanyl, patients were randomly assigned to group ASV or group control. Both protocols were divided into three predefined phases, and weaning progressed according to arterial blood gas and clinical criteria. In phase 1, ASV mode was set at 100% of the theoretical value of volume/minute in group ASV, and synchronized intermittent mandatory ventilation mode was used in group control. When spontaneous breathing occurred, ASV setting was reduced by 50% of minute ventilation (phase 2) and again by 50% (phase 3), and the trachea was extubated. In group control, the ventilator was switched to 10 cm H2O inspiratory pressure support (phase 2), then to 5 cm H2O (phase 3) until extubation.

Results: Forty-nine patients were enrolled. Sixteen patients completed the ASV protocol, and 20 the standard protocol; 7 patients were excluded in group ASV and 6 in group control according to explicit, predefined criteria. There were no differences between groups in perioperative characteristics or in the doses of sedation. The primary outcome of the study, that is, the duration of tracheal intubation, was shorter in group ASV than in group control (median [quartiles]: 3.2 [2.5–4.6] vs. 4.1 [3.1–8.6] h; P < 0.02). Fewer arterial blood analyses were performed in group ASV (median number [quartiles]: 3 [3–4] vs. 4 [3–6]), suggesting that fewer changes in the settings of the ventilator were required in this group.

Conclusions: A respiratory weaning protocol based on ASV is practicable; it may accelerate tracheal extubation and simplify ventilatory management in fast-track patients after cardiac surgery. The evaluation of potential advantages of the use of such technology on patient outcome and resource utilization deserves further studies.

RAPID tracheal extubation is a major component of “fast-track” recovery, progressively becoming a recommended strategy in uncomplicated cardiac surgery. This practice has been demonstrated to be safe in selected patients. It has resulted in reductions in ICU length of stay, hospital length of stay, resource utilization, and cost without adversely affecting mortality and morbidity. Different strategies have been proposed to reduce the duration of mechanical ventilation after cardiac surgery, including use of short-duration anesthetic drugs, standardization of patient care through “clinical pathways,” and a reduction of the duration of cardiopulmonary bypass time and the depth of hypothermia. The extubation time after cardiac surgery is characterized by an optimal “window of opportunity” that is determined by the adequacy of rewarming, control of hemodynamic problems, and postoperative bleeding. However, specific ventilatory strategies aimed at accelerating respiratory weaning after cardiac surgery have received little attention.

Adaptive support ventilation (ASV) is a microprocessor-controlled mode of ventilation that maintains an operator preset, minimum minute ventilation, independent of the patient’s activity. Inspiratory pressure and ventilator rate are adjusted breath by breath to maintain an optimal respiratory pattern (tidal volume and respiratory rate). Previous studies have tested its efficiency, safety, and adaptability in lung models and in patients undergoing general anesthesia during position changes and transition between two- and one-lung ventilation. Adaptive support ventilation appropriately decreased ventilatory support in patients with chronic respiratory failure who tolerated a conventional weaning trial, suggesting that this mode may facilitate respiratory weaning.

We hypothesized that ASV could accelerate respiratory weaning after cardiac surgery. Therefore, we set out to determine whether a weaning protocol based on ASV resulted in a reduction in time to extubation in a randomized controlled trial.

Materials and Methods

After approval from the Ethics Committee of the Faculty of Medicine of the University of Lausanne (Lausanne, Switzerland), preoperative written informed consent was obtained from eligible patients. The study was...
conducted between June 1999 and February 2000 in the surgical ICU of our hospital. All patients scheduled for elective coronary artery bypass grafting under cardiopulmonary bypass were considered for enrollment. The preoperative exclusion criteria were age greater than 75 yr, poor myocardial function (preoperative ejection fraction < 30% by ventriculography), chronic obstructive pulmonary disease necessitating bronchodilator therapy, significant hepatic disease (alanine aminotransferase or aspartate aminotransferase values > 150 U/l), renal failure (creatinine value > 180 \( \mu \)M), or history of seizure and stroke. Clinical preoperative characteristics, including age, sex, Parsonnet cardiac surgery risk score according to Parsonnet et al., and intraoperative data including anesthesia, cardiopulmonary bypass and aortic cross-clamp duration, left ventricular ejection fraction before and after bypass determined by transesophageal echocardiography, fentanyl and midazolam doses, and temperature on arrival in the ICU were recorded.

Patients were assigned at random to two parallel groups, one treated with an ASV-based protocol (group AVS), the other with a standard protocol of respiratory weaning (group control). Each code was indicated on a data form that was sealed in an envelope and opened upon the patient’s arrival in the ICU. After enrollment, the postoperative exclusion criteria included any conditions hindering the fast-track approach. These included severe postoperative hemorrhage (chest tube drainage > 500 ml/h, ≥ 350 ml/h during 2 h, or > 1,000 ml in total), repeat operation, postoperative myocardial ischemia, refractory hypoxemia (ratio of arterial oxygen tension to oxygen inspiratory fraction [\( \text{Pao}_2/\text{FiO}_2 \] < 150 at two arterial blood gas [ABG] analyses at an interval of 20 min each), and neurologic complication precluding the patient’s collaboration.

Clinical Management

Patient management was performed by the attending anesthesiologist and intensivist, and data collected by a research resident (Dr. Sulzer). The patients were anesthetized according to a protocol, including etomidate, fentanyl and vecuronium for induction and midazolam and low-dose fentanyl for maintenance. Cardiopulmonary bypass was performed under moderate hypothermia (28–32°C), using a membrane oxygenator and a nonpulsatile blood flow. At the end of anesthesia, all patients were transferred to the ICU with tracheal intubation, where they were also managed according to a standardized protocol, including fluid resuscitation with normal saline and starch solutions, blood transfusion to maintain hemoglobin concentration (≥ 7.0 g/dl), dopamine and norepinephrine in continuous infusion to achieve mean arterial pressure less than 70 mmHg; and sodium nitroprusside to treat hypertension above a mean arterial pressure of 100 mmHg. The patient’s requirement for analgesia was assessed by the nurse during the entire ICU stay. Morphine was given in a bolus of 1 or 2 mg intravenously, followed by a continuous infusion of 1 or 2 mg/h when the patient complained or expressed autonomic signs (e.g., sweating, tachycardia, hypertension). The boluses were repeated as needed. During phase 1 of respiratory weaning, propofol was given for sedation in boluses of 20 or 30 mg to a Ramsey score of sedation greater than 3 (i.e., responsive to commands). Shivering was treated with 25 mg intravenous pethidine.

Weaning Protocol

The ventilator used during the study was a Galileo with software version GBC 01.202 (Hamilton Medical AG, Rhäzüns, Switzerland). A thorough description of ASV technology has been reported elsewhere. Briefly, the theoretical value of minute ventilation was based on the nomogram of Radford and the patient’s ideal body weight. The initial settings of the ventilator consisted of three parameters: ideal body weight, the percentage of the theoretical value of minute ventilation desired (percentage minute ventilation), and the maximal inspiratory pressure tolerated. The ventilator determines the patient’s respiratory compliance and resistances during an initial test of five breaths and delivers a pressure-controlled ventilation, while optimizing inspiratory pressure and respiratory rate using the formula of Otis. The latter determines the respiratory rate associated with the least work of breathing as a function of the expiratory time constant. As soon as the patient performs an inspiratory effort, which is detected for every breath, the ventilator switches to inspiratory pressure support (IPS). The level of support is continuously adapted to the patient’s respiratory rate and tidal volume to achieve the desired minute ventilation using a favorable breathing pattern. Detrimental patterns such as rapid shallow breathing, excessive dead space ventilation, breath stacking (leading to automatic positive end-expiratory pressure), and excessively large breaths are prevented by adjustments of inspiratory pressure and respiratory rate. Thus, the system continuously adapts the ventilator’s settings to the patient’s needs. Both weaning protocols were divided in three phases designed to follow, in each mode, a similar process, using predefined criteria of poor tolerance to weaning (fig. 1 and appendix).

Upon admission, full ventilatory support (phase 1) was initiated in both groups. In group ASV, the initial ventilator settings were minute ventilation set at 100% of the theoretical value (100% minute ventilation), oxygen inspiratory fraction (\( \text{FiO}_2 \)) of 100%, positive end-expiratory pressure of 4 cm H\textsubscript{2}O (maintained constant until extubation), peak airway pressure of 25 cm H\textsubscript{2}O (peak airway pressure alarm set at 35 cm H\textsubscript{2}O), and flow trigger sensitivity of 2 I/min. An ABG analysis (Rapidlab Model 865 blood gas analyzer; Ciba-Corning Diagnostics AG, Dietlikon, Switzerland) was performed 10 min after con-
Connection to the ventilator to obtain an arterial carbon dioxide tension (PaCO₂) between 38 and 50 mmHg. If PaCO₂ was 38 mmHg or less or more than 50 mmHg, minute ventilation was lowered or respectively increased by 20%. Each modification of the ventilator settings was controlled 10 min later by another ABG analysis. Adjustments were repeated until the PaCO₂ was in the target. FIO₂ was adjusted to maintain an arterial oxygen saturation (SaO₂) of 95% or more. Phase 1 lasted until patients breathed spontaneously at a frequency of 6 breaths/min or greater for 20 min; weaning could progress after ABG values were checked and clinical criteria of poor tolerance were ruled out (appendix). The continuation of weaning was composed of two phases (phases 2 and 3) lasting at least 20 min each. In phase 2, minute ventilation was lowered by 50%. After 20 min, another assessment of the patient was performed. If clinical and ABG criteria indicated poor tolerance to weaning, mechanical ventilation of phase 1 was reinstated and the patient reassessed accordingly. In case of apnea, the patient also returned to phase 1. If ABG and clinical criteria were complied with, the weaning progressed to phase 3, in which IPS was decreased to 5 cm H₂O. At the end of phase 3, the patient was assessed and the trachea extubated according to the criteria described for group ASV.

**Data and Measurements**

In addition to the duration of respiratory weaning, several variables were recorded in the memory of a clinical monitor (Merlin; Hewlett-Packard, Geneva, Switzerland). Respiratory variables included tidal volume...
Table 1. Preoperative and Postoperative Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ASV</th>
<th>Standard</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>16</td>
<td>20</td>
<td>0.9</td>
</tr>
<tr>
<td>Age (yr), median [range]</td>
<td>59.2 ± 8.7</td>
<td>59.7 ± 8.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>12/4</td>
<td>14/6</td>
<td>0.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.2 ± 6.9</td>
<td>170.0 ± 10.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.1 ± 9.8</td>
<td>76.6 ± 13.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.3 ± 3.5</td>
<td>26.6 ± 3.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Parsonnet score</td>
<td>3.0 ± 3.0</td>
<td>4.8 ± 3.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Anesthesia duration (min)</td>
<td>282 ± 36</td>
<td>310 ± 49</td>
<td>0.07</td>
</tr>
<tr>
<td>CPB duration (min)</td>
<td>72 ± 28</td>
<td>87 ± 25</td>
<td>0.1</td>
</tr>
<tr>
<td>Cross-clamping duration (min)</td>
<td>56 ± 27</td>
<td>59 ± 25</td>
<td>0.7</td>
</tr>
<tr>
<td>Fentanyl total dose (µg/kg body weight)</td>
<td>25.2 ± 7.0</td>
<td>26.8 ± 7.9</td>
<td>0.3</td>
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<tr>
<td>Midazolam total dose (mg/kg body weight)</td>
<td>0.12 ± 0.09</td>
<td>0.09 ± 0.07</td>
<td>0.4</td>
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<tr>
<td>Temperature at arrival in ICU (°C)</td>
<td>35.5 ± 0.6</td>
<td>35.6 ± 0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Ejection fraction prebypass (%)</td>
<td>59 ± 12</td>
<td>60 ± 10</td>
<td>0.8</td>
</tr>
<tr>
<td>Ejection fraction postbypass (%)</td>
<td>62 ± 8</td>
<td>65 ± 10</td>
<td>0.5</td>
</tr>
<tr>
<td>ICU length of stay (h, median [quartile])</td>
<td>21.5 [18.6–22.7]</td>
<td>21.2 [17.9–22.2]</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Mean ± SD unless otherwise specified. ASV = adaptive support ventilation; CPB = cardiopulmonary bypass; ICU = intensive care unit.

(tidal volume in milliliters), respiratory rate (counts per minute), and peak inspiratory pressure (peak airway pressure, centimeters of water). Heart rate, invasive arterial pressure, and arterial oxygen saturation (oxygen saturation measured by pulse oximetry) were monitored continuously and recorded every 5 min during the entire ICU stay. Continuous ST segment analysis was performed using derivations II and V₅. The inflection point was determined manually, and measurement of ST depression or elevation was usually performed at 60–80 ms depending on heart rate. When that point fell within the T wave, it was shortened to a minimum of J + 40 ms. Postoperative myocardial ischemia was defined as reversible ST segment changes lasting at least 1 min and involving either a shift from baseline (adjusted for positional changes) of more than 1.0 mm (0.1 mV) of ST segment depression with a slope less than 0, or more than 2.0 mm of ST segment elevation at the J point.¹⁹

The duration of mechanical ventilation, as well as that of all three phases, was recorded; the durations constituted the primary outcome. The secondary outcomes were the amounts of sedative and analgesic drugs administered.

**Statistical Analysis**

The primary outcome variable was the duration of tracheal intubation. All other variables were considered as secondary. Durations of intubation and protocol phases and ICU length of stay were compared by log rank tests and were expressed as median [quartiles]. Nominal variables were compared between groups by chi-square tests. The continuous values are expressed as mean ± SD or median [quartiles]. For continuous variables, the mean values determined for each phase were compared by two-way analysis of variance for the effect of group and time. When the effect of time was significant, the values at each time were compared with the values at the preceding phases with Dunnett tests. When the interaction was significant, comparisons between groups and over time were performed with Scheffé tests. Because of marked bias of the distribution, the number of arterial blood gas analyses performed, as well as the amount of morphine and propofol administered at each phase, was compared by Wilcoxon tests with a modified Bonferroni correction."³²²" P < 0.05 was considered statistically significant for all analyses. Statistical analysis was performed using JMP Statistical software (version 3.5.1; SAS Institute, Cary, NC)."³¹

**Results**

Of 49 patients enrolled in the study, 36 completed the weaning protocol and were considered in the statistical analysis. No patient was withdrawn for protocol failure or violation. Thirteen patients were withdrawn from the study (seven in group ASV vs. six in group control). The reasons were myocardial ischemia (three and two, respectively), hypoxemia (two and four, respectively), stroke (one and none, respectively), and other neurologic problem (one and none, respectively). The occurrence was not different between groups (P = 0.56). The two groups were not different with respect to baseline and perioperative characteristics (table 1).

The duration of mechanical ventilation was shorter in group ASV (193 [149–273] min) than in group control (243 [186–516] min) (P = 0.02). An a posteriori analysis indicated that the power of this comparison was 57%. In this specific group of patients, a log rank test with an α value of 0.05 would have had a 90% probability of detecting a difference between groups of 120 min. The observed reduction in the intubation time was a result of a shortening of phase 1 (114 [78–230] vs. 171 [115–465] min) (P = 0.02), whereas phases 2 and 3 were not different (fig. 2 and table 2).
In a post hoc analysis, considering fast-track success as an extubation within 6 h, we found that 27 patients succeeded, whereas 9 patients failed. More patients had successful extubation within 6 h in group ASV (15 of 16) than in group control (12 of 20) (P < 0.01). No reintubation was required in either group.

The respiratory variables are reported in Table 2. Peak airway pressure was lower in group ASV during phase 1 (17.7 ± 0.5 vs. 20.4 ± 0.4 cm H2O) and in phase 2 (13.1 ± 0.5 vs. 16.0 ± 0.4 cm H2O). There was no difference during phase 3 (12.0 ± 0.5 vs. 12.0 ± 0.4 cm H2O). Tidal volume and respiratory rate were not different between groups. On analyzing the effect of time on all patients, during phase 3 (12.0 ± 0.5 vs. 12.0 ± 0.4 cm H2O), tidal volume and respiratory rate were not different between groups. On analyzing the effect of time on all patients, peak airway pressure (19.1 ± 0.3 vs. 14.5 ± 0.3 cm H2O) and tidal volume (474 ± 9 vs. 448 ± 9 ml) decreased during phase 2, whereas respiratory rate increased (14.3 ± 0.4 vs. 17.3 ± 0.4 breaths/min). During phase 3, peak airway pressure further decreased (14.5 ± 0.3 vs. 12.0 ± 0.3 cm H2O). There was no difference in the mean tidal volume, respiratory rate, and positive end-expiratory pressure, as compared with phase 2. PaCO2 and the ratio of PaCO2 to FiO2 did not differ between groups and over time (table 2). There were more ABG analyses performed in group control (3 [3–4] vs. 4 [3–6]), the difference being observed during phase 1. Intensive care unit length of stay was not different between groups.

The temperature increased from phase 1 to phase 2 similarly in both groups. The hemodynamic variables are reported in Table 2. There were no differences between groups with regard to heart rate and arterial pressure. Heart rate increased significantly from phase 1 to phase 2 but not from phase 2 to phase 3. There was no difference between groups in the doses of propofol, morphine, and pethidine administered.

### Discussion

In the current randomized controlled study of respiratory weaning after uncomplicated cardiac surgery, a protocol based on ASV was compared with a standard one based on SIMV and IPS. The major finding was that the trachea was extubated earlier in group ASV, and this result was related to a reduction of the phase of full ventilatory support.

#### Weaning Strategy

To our knowledge, few studies have evaluated the efficacy of a specific ventilatory strategy to reduce the duration of intubation after fast-track cardiac surgery.22,23 In contrast, the reduction of mechanical ven-
Adaptive Support Ventilation for Weaning

Adaptive support ventilation provides a ventilation in a pressure mode (pressure-controlled ventilation), as well as an automatic switch from pressure-controlled ventilation to IPS. In group ASV, we observed a significant reduction in intubation time that was related to a faster recovery of spontaneous ventilation, as indicated by a shorter phase of controlled ventilation (phase 1). This observation suggests that patient–machine interaction could have been improved in comparison to the SIMV ventilation.

Mechanical ventilation with ASV was possible in all the patients, including those with moderate respiratory failure (PaO₂/FiO₂ ratio between 150 and 300 mmHg), while respecting the limits of inspiratory pressure. The lower number of ABG analyses in group ASV indicates that fewer changes of the respiratory settings were necessary, suggesting that ASV may simplify the management of respiratory weaning.

The effect of different ventilatory modes on clinical outcomes is often difficult to assess. For each mode, a protocol must be implemented that guarantees not only safety but also efficacy during mechanical ventilation and weaning. The criteria for making clinical decisions such as increasing or reducing ventilatory support or extubating the trachea must be detailed and explicit. This guarantees the safety and efficacy of the weaning process and minimizes observer’s bias and variability. Thus, the current study was divided into three phases defined by explicit criteria (fig. 1). The end of each phase was determined by criteria that were identical in both protocols, guaranteeing an objective comparison between the two ventilatory modes.

Limitations of Study

Despite the limited number of patients included in our study, they were randomly assigned to one of two groups. The groups were well matched for nine perioperative variables known to influence the duration of postoperative ventilation (table 1). The number of drop-outs (27%), attributable to conditions known to disturb the fast-track process, may appear substantial. It is unlikely that it invalidates the results because both number and reasons for dropouts were balanced between groups. Published randomized controlled trials on fast-track process after cardiac surgery, using similar inclusion criteria and end points, have reported an incidence of severe adverse events or dropping out ranging from 20 to 40%. In the present study, most adverse events were prospectively defined as exclusion criteria; this could explain the observed rate of dropouts. Therefore, we believe that the results of this preliminary study are valid under the specific conditions of our practice. The lack of difference in ICU length of stay suggests that no major difference in resource utilization occurred, despite a reduction in the number of manipulations of settings. Thus, further investigations including a cost efficiency analysis are required before the precise role of ASV can be firmly established for respiratory weaning after cardiac surgery.

The present study suggests that a weaning protocol based on ASV is practicable and that it may accelerate tracheal extubation in patients who completed a fast-track protocol after cardiac surgery under the condition of cardiopulmonary bypass. This acceleration is related to a faster recuperation of sustained spontaneous ventilation, which might be related to an improved patient–machine interaction. Adaptive support ventilation was also feasible in patients presenting a moderate respiratory failure, a common finding after cardiopulmonary bypass. The evaluation of potential advantages of the use of such technology on patient outcome and resource utilization deserves further studies.
The authors thank Guy Van Melle, Ph.D. (Institute of Social and Preventive Medicine, University of Lausanne, Lausanne, Switzerland), for statistical advice and the nursing team of the surgical intensive care unit for their active collaboration.

References


Appendix

Criteria of Poor Tolerance to Weaning

Mechanical ventilation was returned to the previous step if any of the following occurred:

- respiratory rate ≥ 35 breaths/min
- arterial oxygen saturation < 90%
- heart rate > 140 beats/min or a sustained increase or decrease in the heart rate of more than 20%
- systolic blood pressure > 200 mmHg or < 90 mmHg
- agitation
- diaphoresis
- arterial carbon dioxide tension (PaCO2) > 50 mmHg

Tracheal Extubation Criteria

Extubation was performed when all of the following were present:

- patient responsive and cooperative
- oxygen inspiratory fraction (FiO2) ≤ 50%; positive end-expiratory pressure = 5 cm H2O, ratio of arterial oxygen tension (PaO2) to FiO2 > 150
- hemodynamically stable, well perfused, urine output >0.5 ml·kg⁻¹·h⁻¹
- chest tube drainage < 200 ml in the last hour
- absence of uncontrolled arrhythmia
- rectal temperature > 36.0°C

Reintubation Criteria

Reintubation was performed if any of the following were present: Respiratory causes:

- acute respiratory failure: PaO2 > 60 mmHg with FiO2 ≥ 60% by mechanical ventilation; PaCO2 > 50 mmHg and pH < 7.30
- respiratory rate > 40 breaths/min with physical signs of distress

Nonrespiratory causes:

- acute deterioration of level of consciousness or new onset of global neurologic deficit
- inability to protect the airway from aspiration of oropharyngeal secretions and gastric contents because of neurologic dysfunction or altered level of consciousness
- severe hemodynamic instability or cardiogenic shock

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