A Randomized Controlled Trial of Adaptive Support Ventilation Mode to Wean Patients after Fast-track Cardiac Valvular Surgery

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ABSTRACT

Background: Adaptive support ventilation can speed weaning after coronary artery surgery compared with protocolized weaning using other modes. There are no data to support this mode of weaning after cardiac valvular surgery. Furthermore, control group weaning times have been long, suggesting that the results may reflect control group protocols that delay weaning rather than a real advantage of adaptive support ventilation.

Methods: Randomized (computer-generated sequence and sealed opaque envelopes), parallel-arm, unblinded trial of adaptive support ventilation *versus* physician-directed weaning after adult fast-track cardiac valvular surgery. The primary outcome was duration of mechanical ventilation. Patients aged 18 to 80 yr without significant renal, liver, or lung disease or severe impairment of left ventricular function undergoing uncomplicated elective valve surgery were eligible. Care was standardized, except postoperative ventilation. In the adaptive support ventilation group, target minute ventilation and inspired oxygen concentration were adjusted according to blood gases. A spontaneous breathing trial was carried out when the total inspiratory pressure of 15 cm H_2O or less with positive end-expiratory pressure of 5 cm H_2O. In the control group, the duty physician made all ventilatory decisions.

Results: Median duration of ventilation was statistically significantly shorter ($P = 0.013$) in the adaptive support ventilation group (205 [141 to 295] min, n = 30) than that in controls (342 [214 to 491] min, n = 31). Manual ventilator changes and alarms were less common in the adaptive support ventilation group, and arterial blood gas estimations were more common.

Conclusion: Adaptive support ventilation reduces ventilation time by more than 2 h in patients who have undergone fast-track cardiac valvular surgery while reducing the number of manual ventilator changes and alarms. **(ANESTHESIOLOGY 2015; 122:832-40)**

ADAPTIVE support ventilation (ASV) is a closed-loop mode of ventilation in which the ventilator adjusts the inspiratory pressure to achieve a tidal volume that minimizes the work of breathing based on the Otis equation. In addition, the ventilator switches between control and supports breaths based on the presence or absence of spontaneous breathing effort. Previous studies have demonstrated that automated weaning using ASV mode results in faster[1,2] or equivalent weaning time[3] after fast-track coronary artery bypass surgery compared with protocolized weaning using synchronized intermittent mandatory ventilation (SIMV) with pressure support[2,3] or pressure-regulated volume control with automode.[1] However, there are no studies examining automated weaning in patients undergoing valvular surgery. Morbidity and mortality are higher in this group, and they are forming an increasingly large proportion of cardiac surgical patients.[4] Despite this, there is a dearth of data on fast-track cardiac valvular surgery. Almost all randomized controlled trials of patients undergoing fast-track cardiac surgery have focused on coronary artery bypass surgery

What We Already Know about This Topic

- Adaptive support ventilation is a closed-loop mode of ventilation in which the ventilator adjusts the inspiratory pressure to achieve a tidal volume that minimizes the work of breathing
- This study determined whether adaptive support ventilation is associated with a shorter duration of ventilation compared with physician-directed weaning in patients undergoing elective fast-track cardiac valvular surgery

What This Article Tells Us That Is New

- Use of closed-loop weaning with adaptive support ventilation results in more rapid weaning of patients after cardiac valvular surgery than did physician-directed weaning, without an increase in morbidity

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predominantly[5] or exclusively.[1–3,6–23] In one study, half the patients underwent valvular surgery.[24] Thus, it is important to study the effect of different weaning modalities in this group, rather than simply extrapolating from studies of patients undergoing coronary artery bypass grafting.

We hypothesized that in patients undergoing elective fast-track cardiac valvular surgery, ASV would be associated with a shorter duration of ventilation compared with physician-directed weaning and carried out an unblinded, randomized, controlled, parallel-arm trial to test this hypothesis.

Materials and Methods

The study was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee and registered at the Centre for Clinical Trials of The Chinese University of Hong Kong, Hong Kong, China (CUHK CCT00308). Written informed consent was obtained from all participants.

The study was carried out in the 22-bed adult multidisciplinary intensive care unit (ICU) of a 1,400-bed tertiary referral university hospital. The ICU is the sole adult ICU in the hospital. Cardiac surgical patients receive 1:1 nursing at all times. The unit was staffed with six doctors (of whom approximately half were intensive care specialists) during the day and two resident doctors (one of whom was an anesthesiology or intensive care specialist), with a further intensive care specialist available for consultation at night.

All patients scheduled for elective cardiac valvular surgery between May 2012 and March 2013 were screened for eligibility. Patients undergoing isolated valve surgery and those undergoing valve surgery combined with another cardiac surgical procedure were included. Preoperative exclusion criteria were acute or chronic obstructive pulmonary disease, serum creatinine concentration greater than 200 μmol/l, serum aspartate transaminase concentration greater than 80 U/l, left ventricular ejection fraction less than 30%, history of seizures or stroke, and age older than 80 yr or younger than 18 yr. Postoperative exclusion criteria were chest tube drainage greater than 500 ml/h, reoperation, myocardial infarction, need for high-dose inotropes or vasopressors or intraaortic balloon pump, and refractory hypoxemia with an arterial oxygen tension to fractional inspired oxygen concentration ratio less than 150 mmHg.

Patients were randomized to receive and be weaned using ASV or be ventilated and weaned as directed by duty clinicians (control group). Simple randomization with 1:1 allocation was carried out according to a computer-generated sequence using sealed opaque envelopes which were opened after the patient's arrival to the ICU. The clinical trial design was a parallel-arm design. The CONSORT diagram (fig. 1) details the results of screening and randomization.

Patients were premedicated with oral midazolam 0.1 to 0.2 mg/kg unless contraindicated. Anesthesia was induced with various combinations of IV fentanyl 2 to 10 μg/kg, IV midazolam 20 to 50 μg/kg, supplemented with propofol up to 50 mg, and/or sevofluvane up to end-tidal concentration of 6.0%. Paralysis was achieved using IV rocuronium 1 mg/kg. Patients were intubated after induction and paralysis and were ventilated with oxygen-enriched air using volume-controlled ventilation with automatic adjustment of flow to minimize airway pressure, with tidal volume of 8 to 10 ml/kg actual body weight and positive end-expiratory pressure of 5 cm H_2O at a frequency of 12 breaths/min. These were adjusted to maintain an end-tidal carbon dioxide tension of 30 to 35 mmHg. During cardiopulmonary bypass, ventilation was stopped, and 5 to 10 cm H_2O of continuous positive pressure was applied to the lungs. Anesthesia was maintained with a combination of IV propofol (0 to 8 mg kg^{-1} h^{-1}) and IV remifentanil (0 to 0.2 μg kg^{-1} min^{-1}) to keep the bispectral index scale between 40 and 60. Boluses of IV fentanyl 50 to 100 μg were given as needed for intense stimulation and on rewarming. Atracurium was infused at 0.3 mg/kg per minute IV to provide muscle relaxation. IV morphine 0.1 to 0.3 mg/kg was given to provide intraoperative and postoperative analgesia. For hemodynamic fluctuations unrelated to depth of anesthesia, IV administration of phenylephrine 50 to 100 μg, ephedrine 6 mg, metoprolol 1 mg, glyceryl trinitrate infusion, atropine 0.3 mg, inotropes, or fluid boluses were used according to the clinical situation.

Surgery was carried out using standard procedures through a median sternotomy by a single surgical team.

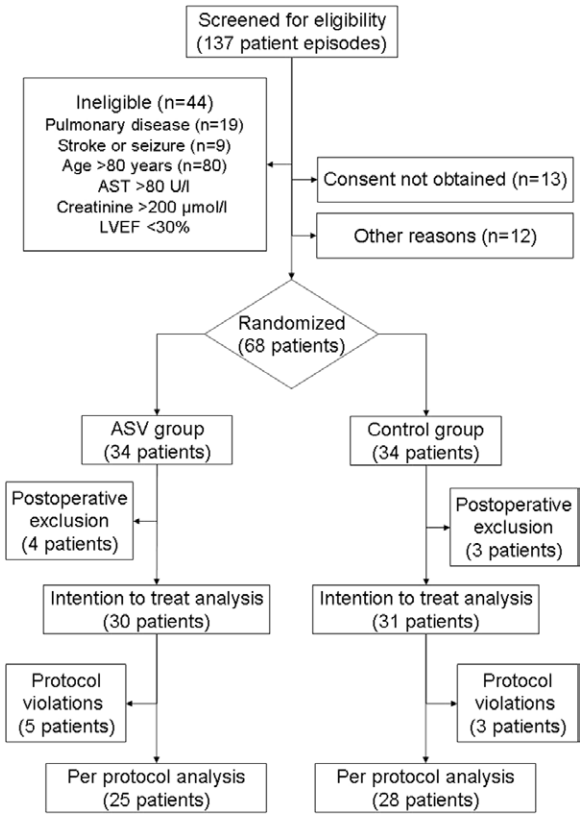

Fig. 1. CONSORT diagram. AST = aspartate transaminase; ASV = adaptive support ventilation; LVEF = left ventricular ejection fraction.

Mechanical or bioprosthetic valves were used for valve replacement at the discretion of the surgical team.

After surgery, the patients were transferred to the ICU sedated with propofol (1 to 2 mg kg^{-1} h^{-1}). On arrival in the ICU, paralysis was reversed if necessary (based on train of four) with neostigmine, and sedation was stopped. Patients were managed according to standard unit protocols except for mechanical ventilation. In brief, arterial blood pressure, central venous pressure, electrocardiogram, and pulse oximetry were monitored continuously. Normal saline, lactated Ringer's solution, and gelatin-based colloid solutions were used for fluid resuscitation. Hemoglobin concentrations were maintained 8 g/dl or greater. Dopamine or epinephrine was used to maintain mean arterial pressure 60 mmHg or greater and glyceryl trinitrate and sodium nitroprusside to treat hypertension (mean arterial pressure ≥100 mmHg). The bedside nurses assessed analgesic requirements and gave boluses of 1 to 2 mg morphine to a total of 10 mg on patient request if fully awake or if still sedated when hypertensive and restless.

All patients were ventilated with a Hamilton-G5 ventilator (Hamilton Medical GA, Rhäzuns, Switzerland; software version 2.1X). Patients randomized to the ASV group were managed according to the algorithm in figure 2. If the patient was not successfully weaned within 8 h, the weaning protocol was discontinued, and ventilatory management was directed by duty physicians.

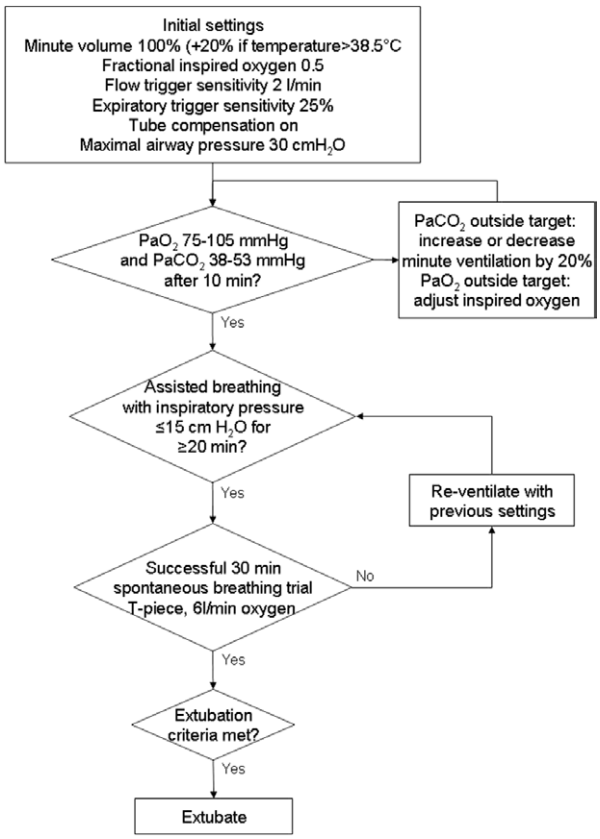

Fig. 2. Weaning protocol for adaptive support ventilation group.

Ventilation of patients in the control group was managed at the duty physicians' discretion. Patients in both groups were assessed for extubation when the bedside nurse observed that they met the following criteria: responsive and cooperative; F_{IO_2} less than 40%; P_{AO_2}/F_{IO_2} more than 150; positive end-expiratory pressure less than or equal to 5 cm H_2O; hemodynamically stable; urine output exceeds 0.5 ml kg^{-1} h^{-1}; the last hour chest tube drainage less than 100 ml; no uncontrolled arrhythmia; and rectal temperature is above 36.0°C. If these criteria were fulfilled, the physician on duty was notified to assess and extubate the patient.

The primary endpoint of the study was duration of mechanical ventilation in the ICU. Secondary endpoints were duration of intubation in the ICU, duration of ICU stay, duration of hospital stay, postoperative complications, and mortality. Other data collected are listed in tables 1–7.

Statistical Analysis

The sample size was calculated by PASS 11.0 (NCSS, Kaysville, UT). From a previous study of ASV in patients undergoing coronary artery bypass surgery and managed postoperatively in our unit,[1] we estimated the duration of ventilation would be 300 min with an interquartile range of 205 to 365 min. Based on this estimate, an effect size of 90-min reduction in duration of ventilation, power of 80%, a trial designed to demonstrate superiority and statistical significance threshold of *P* value less than 0.05, we calculated that a total of 56 patients would be required. Allowing for a 20% dropout rate, we planned to recruit 68 patients in total.

Parametric continuous data are expressed as mean (SD), nonparametric continuous data are presented as median (interquartile range), and categorical data as number (%).

The Shapiro–Wilk test was used to check data for normality. Student *t* test (independent sample) and Mann–Whitney U test were used for continuous parametric and nonparametric variables, respectively. In particular, the difference in primary outcome (duration of mechanical ventilation) was analyzed using the Mann–Whitney U test, and the median difference (95% CIs) in duration of mechanical ventilation was estimated using quartile regression. Chi-square or Fisher exact tests were used for categorical data. To compare the ventilator settings and arterial blood gas between both groups during several time points, generalized estimating equation analysis with gamma distribution and exchangeable correlation was applied. All tests were two tailed, and *P* value less than 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS 18.0 for Windows (IBM, Chicago, IL). Data were analyzed on an intention-to-treat basis and per-protocol basis.

Results

Details of number of patients screened, randomized, excluded postoperatively, and analyzed are shown in the CONSORT diagram (fig. 1). Thirty-four patients were randomized to each group. Four patients in the ASV group were excluded

Table 1. Demographics and Preoperative Clinical Variables

Parameters	Group		*P* Value
	ASV (n = 30)	Control (n = 31)	
Female sex, n (%)	10 (33.3)	10 (32.3)	0.929
Age, yr	58 (54–63)	58 (54–64)	0.665
Body height, cm	163 ± 10	163 ± 8	0.944
Body weight, kg	61 ± 10	65 ± 14	0.314
Preoperative aspartate transaminase, IU/l	23 (18–29)	29 (19–38)	0.111
Preoperative creatinine, μmol/l	85 ± 19	84 ± 20	0.804
Forced expiratory volume in 1 s/forced vital capacity, %	81 ± 9	80 ± 7	0.638
Left ventricular ejection fraction category			0.473
Good, n (%)	27 (90)	25 (81)	
Fair, n (%)	3 (10)	6 (19)	
American Society of Anesthesiologists grade			0.787
Grade I to II, n (%)	5 (17)	6 (19)	
Grade III to IV, n (%)	25 (83)	25 (81)	
Comorbidities			
Hypertension, n (%)	10 (33)	8 (26)	0.519
Diabetes mellitus, n (%)	2 (7)	4 (13)	0.671
Liver disease, n (%)	0 (0)	1 (3)	1.000
Renal insufficiency, n (%)	0 (0)	0 (0)	—
Pulmonary hypertension, n (%)	1 (3.3)	0 (0)	0.492
Extracardiac arteriopathy, n (%)	0 (0)	0 (0)	—
Atrial fibrillation, n (%)	7 (23)	16 (52)	0.023
Chronic heart failure, n (%)	7 (23)	10 (32)	0.437
Acute Physiology and Chronic Health Evaluation II score	13 ± 4	12 ± 4	0.401
Logistic European System for Cardiac Operative Risk Evaluation	2.7 (2.1–5.0)	2.7 (1.5–5.5)	0.581
Valve surgery only, n (%)	27 (90)	29 (94)	0.614
Mitral valve replacement only, n (%)	7 (23)	8 (26)	
Mitral and aortic valve replacement, n (%)	4 (13)	1 (3)	
Mitral and aortic valve replacement and tricuspid valve repair, n (%)	0 (0)	2 (7)	
Mitral valve replacement and aortic valve repair, n (%)	1 (3)	1 (3)	
Mitral valve replacement and tricuspid valve repair, n (%)	3 (10)	2 (7)	
Mitral valve repair only, n (%)	1 (3)	6 (19)	
Mitral valve repair and aortic valve replacement, n (%)	2 (7)	0 (0)	
Mitral and tricuspid valve repair, n (%)	3 (10)	2 (7)	
Aortic valve replacement only, n (%)	6 (20)	6 (19)	
Tricuspid valve replacement only, n (%)	0 (0)	1 (3)	
Valve and other surgery, n (%)	3 (6)	2 (0)	
Mitral valve replacement and atrial septal defect closure, n (%)	0 (0)	1 (3)	
Mitral valve replacement, tricuspid valve repair, atrial fibrillation ablation, n (%)	1 (3)	0 (0)	
Mitral and tricuspid valve repair and coronary artery bypass grafting, n (%)	1 (3)	0 (0)	
Mitral valve repair and coronary artery bypass grafting, n (%)	1 (3)	0 (0)	
Aortic valve replacement and coronary artery bypass grafting, n (%)	0 (0)	1 (3)	
Complex surgery,* n (%)	16 (53)	10 (32)	0.096

Values are expressed as mean ± SD, median (interquartile range), or number (%).

* Complex surgery defined as double valve or triple valve surgery, valve combined with coronary artery bypass grafting, or other surgery.

ASV = adaptive support ventilation.

Table 2. Intraoperative Parameters of All Patients

Parameters	Group		*P* Value
	ASV (n = 30)	Control (n = 31)	
Duration of operation, min	203 (180–235)	200 (170–228)	0.578
Duration of anesthesia, min	253 (222–287)	245 (227–272)	0.634
Duration of bypass time, min	125 ± 39	113 ± 32	0.202
Duration of aortic clamping time, min	85 ± 27	72 ± 27	0.053
Total intraoperative use of anesthetics			
Midazolam, mg/kg	0.05 (0.04–0.08)	0.06 (0.05–0.09)	0.308
Propofol, mg/kg	7.7 ± 3.0	6.3 ± 1.5	0.044
Atracurium, mg/kg	1.1 ± 0.3	1.0 ± 0.3	0.252
Rocuronium, mg/kg	0.9 ± 0.2	1.0 ± 0.2	0.143
Fentanyl, μg/kg	10.9 ± 2.9	10.3 ± 3.7	0.510
Remifentanil, μg/kg	0 (0–1.14)	0 (0–2.43)	0.895
Morphine, μg/kg	163 ± 72	139 ± 81	0.235

Values are expressed as mean ± SD or median (interquartile range).
ASV = adaptive support ventilation.

Table 3. Primary Outcomes and Secondary Outcomes Analyzed by Intention-to-treat and per Protocol

Parameters	Group		*P* Value
	ASV	Control	
Intention-to-treat analysis			
Numbers analyzed	30	31	
Time to extubation, min	295 (196–413)	421 (297–653)	0.036
Duration of mechanical ventilation, min	205 (141–295)	342 (214–491)	0.013
Duration of spontaneous ventilation, min	54 (41–91)	71.5 (17–124)	0.921
Length of stay in ICU, h	21 (18–22)	22 (18–23)	0.255
Length of stay in hospital, d	10.5 (9–14.25)	11 (9–16)	0.727
Postoperative length of stay in hospital, d	9 (7.75–11.25)	8 (8–12)	0.826
Early extubation (<8 h), n (%)	24 (80)	19 (61)	0.093
Per-protocol analysis			
Numbers analyzed	25	28	
Time to extubation, min	295 (196–370)	421 (309–656)	0.017
Duration of mechanical ventilation, min	218 (141–295)	342 (219–479)	0.018
Duration of spontaneous ventilation, min	54 (43–91)	72 (19–121)	0.979
Length of stay in ICU, h	21 (19–22)	22 (18–23)	0.382
Length of stay in hospital, d	11 (9–15)	10.5 (9–14)	0.693
Postoperative length of stay in hospital, d	9 (8–12)	8 (8–10)	0.350
Early extubation (<8 h), n (%)	21 (84)	18 (64)	0.104

Values are expressed as median (interquartile range) or number (%).
ASV = adaptive support ventilation; ICU = intensive care unit.

postoperatively because of hemodynamic instability (one patient), reoperation (one patient), and seizures (two patients). Three patients in the control group were similarly excluded because of cardiac arrest, reoperation, and seizure (one patient each). As a result, 30 patients in the ASV group and 31 patients in the control group were included in the intention-to-treat analysis. Protocol violations occurred in five patients in the ASV group (propofol not stopped promptly) and three patients in the control group (propofol not stopped promptly in two patients and ventilated using a different ventilator in one), leaving 25 patients (ASV group) and 28 patients (control group) in the per-protocol analysis. All analyses presented were based on complete data except for hemodynamic data and ventilatory data.

Demographic, preoperative, and intraoperative parameters were comparable in the two groups except for an increased total dose of propofol and a trend to increased aortic cross clamp time and complex surgery in the ASV group and an increased prevalence of preoperative atrial fibrillation in the control group (tables 1 and 2).

Duration of mechanical ventilation and intubation was statistically significantly shorter in the ASV group than that in the control group. On an intention-to-treat analysis, duration of mechanical ventilation was reduced from a median of 342 min to a median of 205 (table 3). Median difference in duration of mechanical ventilation was 137 min (95% CI, 26 to 248).

Table 4. Intensive Care Management in Patients Who Completed the Study per Protocol

Parameters	ASV (n = 25)	Control (n = 28)	*P* Value
Total number of arterial blood gas samples	6 (5–7)	5 (4–5)	0.006
Total number of alarms	11 (7–30)	27 (14–57)	0.016
Numbers of manual settings	2 (1–5)	4 (2–5)	0.047
Temperature on ICU admission, °C	36.1 ± 0.4	36.1 ± 0.6	0.501
Total dose of morphine, mg	7.0 (3.0–10.0)	7.0 (5.0–9.0)	0.858
Fluid balance during first 24 h of ICU stay, ml	419 ± 522	404 ± 654	0.926
Lowest pulse oximetry value during weaning, %	98 (97–99)	98 (97–99)	0.805

Values are expressed as mean ± SD or median (interquartile range).
ASV = adaptive support ventilation; ICU = intensive care unit.

Table 5. Arterial Blood Gas and Hemodynamic Changes between ASV and Control Groups during the Process of Weaning and Extubation of Patients Completed Study per Protocol

Parameters	Group	Baseline	During Mechanical Ventilation	During Spontaneous Ventilation	After Extubation	n	*P* for Group	*P* for Interaction
pH	ASV	7.39 ± 0.05	7.37 ± 0.04	7.36 ± 0.04	7.35 ± 0.08	25	0.349	0.858
	Control	7.39 ± 0.06	7.37 ± 0.05	7.37 ± 0.05	7.37 ± 0.03	28		
Arterial carbon dioxide tension, mmHg	ASV	41 ± 6	44 ± 6	44 ± 6	44 ± 7	25	0.539	0.968
	Control	41 ± 8	42 ± 8	43 ± 10	43 ± 6	28		
Arterial oxygen tension, mmHg	ASV	203 ± 102	133 ± 35	170 ± 58	176 ± 69	25	0.114	0.200
	Control	178 ± 77	132 ± 39	144 ± 57	149 ± 41	28		
Arterial bicarbonate concentration, mmol/l	ASV	24.2 ± 2.3	24.3 ± 2.5	24.3 ± 2.8	23.7 ± 3.4	25	0.653	0.672
	Control	23.2 ± 2.8	24.0 ± 2.4	24.0 ± 3.6	24.1 ± 3.0	28		
Heart rate, beats/min	ASV	79 ± 9	81 ± 9	79 ± 11	79 ± 9	24	0.640	0.481
	Control	77 ± 6	79 ± 8	80 ± 10	80 12	28		
Systolic blood pressure, mmHg	ASV	123 ± 14	121 ± 17	114 ± 12	113 ± 13	24	0.673	0.217
	Control	121 ± 13	119 ± 13	118 ± 13	119 ± 10	28		
Diastolic blood pressure, mmHg	ASV	68 ± 11	65 ± 8	61 ± 7	60 ± 8	24	0.588	0.400
	Control	65 ± 9	63 ± 6	61 ± 6	61 ± 6	28		

Values are expressed as mean ± SD.

On per-protocol analysis, use of ASV was associated with statistically significantly fewer manual ventilator adjustments (median of 2 *vs.* 4) and ventilator alarms (11 *vs.* 27) but one additional blood gas sample (6 *vs.* 5) (table 4).

There were no differences between the two groups (per-protocol analysis) in terms of respiratory, ventilatory, or hemodynamic variables except that peak pressures and tidal volumes were slightly higher in the control group (tables 5 and 6). Hemodynamic data for one patient in the per-protocol ASV group and inspired oxygen data for one patient in the per-protocol control group were lost due to a computer error. There were no statistically or clinically significant differences in the incidence of postoperative complications (table 7). Two patients in the ASV group required reintubation: one for an esophageal perforation and one because of a seizure. The patient with the esophageal perforation died on the 28th postoperative day.

In the control group, all but three patients were ventilated in volume-preset SIMV with pressure support with constant flow (SIMV breaths). Two were ventilated in constant-flow volume-preset assist control mode and one in pressure-preset SIMV with pressure support. All patients were subsequently changed to pressure support mode after a median of 207.5 (104 to 300) min. The majority of patients underwent an unassisted breathing trial before extubation, but four were extubated from pressure support ventilation.

Discussion

Our results demonstrate that closed-loop weaning of fast-track cardiac surgical patients after valvular surgery using ASV is statistically significantly faster than weaning directed by physicians. This is in keeping with previous results in fast-track patients who had undergone coronary artery bypass grafting, in whom weaning in ASV mode is as fast or faster

Table 6. Ventilatory Data for Patients Who Completed Study per Protocol

Parameters	Group	Baseline	First 20 Min of Mechanical Ventilation	During Mechanical Ventilation	Last 20 Min of Mechanical Ventilation	n	*P* for Group	*P* for Interaction
Fractional inspired oxygen, %	ASV	49 ± 2	45 ± 5	42 ± 6	41 ± 6	25	0.897	0.001
	Control	45 ± 5	46 ± 6	43 ± 5	43 ± 5	27		
Respiratory rate, breaths/min	ASV	14 ± 1	15 ± 4	15 ± 4	14 ± 2	25	0.620	0.040
	Control	14 ± 1	15 ± 3	15 ± 5	15 ± 4	28		
Tidal volume, ml/predicted body weight	ASV	7.5 ± 0.5	7.7 ± 0.9	8.6 ± 1.2	9.0 ± 1.3	25	0.431	0.038
	Control	8.0 ± 1.3	8.0 ± 1.4	9.0 ± 2.0	8.8 ± 2.0	28		
Minute ventilation, ml/min	ASV	5,960 ± 450	6,350 ± 1,200	7,180 ± 1,370	6,860 ± 1,010	25	0.230	0.715
	Control	6,490 ± 970	6,810 ± 1,170	7,324 ± 1,790	7,250 ± 2,420)	28		
Peak airway pressure, cm H_2O	ASV	16 ± 2	17 ± 2	15 ± 2	14 ± 2	25	<0.001	0.222
	Control	19 ± 1	20 ± 4	17 ± 1	16 ± 3	28		
Mean airway pressure, cm H_2O	ASV	9 ± 1	9 ± 1	8 ± 1	7 ± 1	25	0.517	<0.001
	Control	9 ± 1	9 ± 1	8 ± 1	8 ± 1	28		
Positive end-expiratory pressure, cm H_2O	ASV	5.0 ± 0.1	5.0 ± 0.1	5.0 ± 0	5.0 ± 0	25	0.072	0.804
	Control	5.0 ± 0.1	5.1 ± 0.1	5.1 ± 0.5	5.1 ± 0.6	28		

Fractional inspired oxygen data for one patient in the control group were lost. Values are expressed as mean ± SD.

than weaning using a variety of other modes, such as SIMV, pressure-regulated volume control and pressure control. However, the median time to extubation in the ASV arms of these studies is 2.7 to 5 h.[1–3] This is long compared with extubation times in cardiac surgical patients in which early extubation has been targeted,[5,13,19] raising the possibility that the studies should be interpreted not as ASV decreasing the time to extubation compared with other modes, but increasing it less. Further support for this possibility comes from the study by Gruber *et al.*.[1] In this study, protocolized weaning was abandoned in those patients who failed to be weaned using ASV or pressure-regulated volume control with automode within 8 h. Weaning was then left to the clinician's discretion. All these patients were successfully extubated within 30 min of abandoning protocolized weaning. In our study, control group weaning was at the discretion of the physician, suggesting that ASV led to a real improvement in speed of weaning.

The use of a control group in which physicians direct weaning has the advantage that it more closely reflects the real-life clinical situation. However, there are a number of disadvantages. First, the impossibility of blinding ventilation studies leaves open the possibility that the clinicians deliberately slowed weaning in the control group. We believe that this is unlikely. The ICU in which the study was conducted is the sole adult ICU for a 1,400-bed tertiary referral university hospital. Despite this, the ICU only has 22 staffed beds. There is, therefore, constant pressure to wean patients as soon as possible so that they can be discharged if necessary. Second, the clinicians may have been too busy to wean the patients in the control group. Again, we believe this is unlikely. Postoperative cardiac surgical patients are usually admitted to the ICU during office hours, when the medical staffing of the ICU was high both in terms of number of doctors and their seniority.

The most common mode of weaning in the control group was SIMV. Studies in patients ventilated for more than 1 week have demonstrated that this is an inferior mode of weaning,[25,26] and it is possible that the results of our study simply reflect the inferiority of SIMV rather than the superiority of ASV. However, the population of patients ventilated for 1 week is very different to our study population, and these data are not directly applicable to our patients.

Our study was a single-center study and, although adequately powered, involved a relatively small number of patients. Therefore, caution should be applied in extrapolating our results to other settings. In particular, we believe that the level of staffing may be an important factor in determining the degree of benefit from closed-loop weaning. A multicenter study of closed-loop weaning using SmartCare® (Draeger Medical, Lubeck, Germany) found that closed-loop weaning resulted in more rapid weaning,[27] whereas a similar study carried out in an extremely well-staffed unit demonstrated no benefit.[28]

There was an imbalance in baseline characteristics between our groups with a higher prevalence of preoperative atrial fibrillation in the control group. Although we cannot exclude the possibility that this difference explains the longer ventilation time in the control group, we think this is unlikely, and any effect of atrial fibrillation will have been balanced, to some extent, by a higher dose of propofol and the trend to longer aortic cross clamp time and more complex surgery in the ASV group.

The peak airway pressure was slightly, but statistically significantly, higher in the control group. This is consistent with the use of volume-preset SIMV with pressure support with constant flow during SIMV breaths in the majority of control group patients. In ASV, the inspiratory pressure is constant within a breath.

Table 7. Complications and Clinical Outcomes Analyzed by Intention-to-treat and per Protocol

Parameters	ASV	Control	*P* Value
Intention-to-treat analysis			
Numbers analyzed	30	31	
Readmission to ICU, n (%)	1 (3.3)	0 (0)	0.492
Reoperation, n (%)	1 (3.3)	1 (3.2)	1.000
Arrhythmia requires intervention, n (%)	13 (43.3)	11 (35.5)	0.530
Reintubation, n (%)	2 (6.7)	0 (0)	0.238
Pulmonary complications require intervention, n (%)	4 (13.3)	7 (22.6)	0.348
Infective complications, n (%)	5 (16.7)	6 (19.4)	0.785
Gastrointestinal complications, n (%)	1 (3.3)	0 (0)	0.492
New postoperative stroke, n (%)	1 (3.3)	0 (0)	0.492
New hemofiltration and dialysis, n (%)	1 (3.3)	0 (0)	0.492
Hospital mortality, n (%)	1 (3.3)	0 (0)	0.492
Per-protocol analysis			
Numbers analyzed	25	28	
Readmission to ICU, n (%)	1 (4.0)	0 (0.0)	0.472
Reoperation, n (%)	1 (4.0)	1 (3.6)	1.000
Arrhythmia requires intervention, n (%)	11 (44.0)	10 (35.7)	0.538
Reintubation, n (%)	2 (8.0)	0 (0.0)	0.218
Pulmonary complications require intervention, n (%)	4 (16.0)	7 (25.0)	0.420
Infective complications, n (%)	5 (20.0)	6 (21.4)	0.898
Gastrointestinal complications, n (%)	1 (4.0)	0 (0.0)	0.472
New postoperative stroke, n (%)	1 (4.0)	0 (0.0)	0.472
New hemofiltration and dialysis, n (%)	1 (4.0)	0 (0.0)	0.472
Hospital mortality, n (%)	1 (4.0)	0 (0.0)	0.472

Values are expressed as numbers of cases and percentage within group.

A recent meta-analysis of closed-loop weaning concluded that there was no benefit from closed-loop weaning in the surgical subgroup of patients.[29] However, the analysis included studies of a more heterogeneous group of surgical ICU patients. In particular, a substantial weighting was given to a study of non–fast-track cardiac surgical patients in which 50% of patients were not extubated by 16 h. The authors of that study speculated that patients were left intubated because the unit policy was to discharge patients from the ICU on the morning after surgery at the earliest.[30] When the focus is limited to ASV and fast-track cardiac surgical patients, the results of this current study and two previous studies show a reduction in ventilation time compared with other modes of weaning,[1,2] with one further study showing no difference.[3]

Use of ASV was also associated with a reduction in the number of manual changes of ventilator settings and the number of ventilator alarms, at the cost of one additional arterial blood gas analysis. Finding adequate numbers of staff is a problem in many ICUs and a ventilatory mode that reduces workload is an advantage.

Length of ICU and hospital stay was not altered by use of ASV. This is not surprising as there are many other factors which determine length of stay. However, in the context of a postoperative care pathway designed to maximize efficient use of intensive care resources, use of ASV may provide an important operational advantage. Van Mastrigt *et al.* randomized cardiac surgical patients to short intensive care stay (8 h) or conventional (overnight) ICU stay. The ICU readmission rate and postoperative morbidity were similar in the two groups, but the improvement in quality of life was higher in the short stay group and the cost was lower. Of the 300 patients randomized to short stay, 161 were able to be discharged from ICU within 8 h. The median time to extubation was 6.5 h.[20] Among our ASV group, the median time to extubation was 4.9 h, and 80% of patients were extubated in less than 8 h. This suggests that the proportion of patients who are ready for discharge at 8 h may be increased by use of ASV and thus the savings may be greater.

Postoperative complications did not differ between groups, and the incidence of complications was within the range expected for cardiac surgery. This suggests that the shorter ventilation time associated with use of ASV does not come at the cost of increased complications and that fast-track postoperative care of patients undergoing cardiac valvular surgery can be safely carried out.

In conclusion, use of closed-loop weaning with ASV results in more rapid weaning of patients after cardiac valvular surgery than did physician-directed weaning, without an increase in morbidity. This may facilitate early discharge from the ICU, which has been shown to decrease cost and improve quality of life without increased postoperative morbidity.[20]

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Competing Interests

Dr. Gomersall has received funding for travel to speak at two conferences from Hamilton Medical GA, Rhäzuns, Switzerland. The other authors declare no competing interests.

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References

1. Gruber PC, Gomersall CD, Leung P, Joynt GM, Ng SK, Ho KM, Underwood MJ: Randomized controlled trial comparing adaptive-support ventilation with pressure-regulated volume-controlled ventilation with automode in weaning patients after cardiac surgery. Anesthesiology 2008; 109:81–7

2. Sulzer CF, Chioléro R, Chassot PG, Mueller XM, Revelly JP: Adaptive support ventilation for fast tracheal extubation after cardiac surgery: A randomized controlled study. Anesthesiology 2001; 95:1339–45
3. Petter AH, Chioléro RL, Cassina T, Chassot PG, Müller XM, Revelly JP: Automatic "respirator/weaning" with adaptive support ventilation: The effect on duration of endotracheal intubation and patient management. Anesth Analg 2003; 97:1743–50
4. Bridgewater B, Gummerton J; on behalf of the European Association for Cardio-Thoracic Surgery: Fourth EACTS Adult Cardiac Surgical Database Report. Oxford, United Kingdom, Dendrite Clinical Systems Ltd., 2010
5. Pettersson PH, Settergren G, Owall A: Similar pain scores after early and late extubation in heart surgery with cardiopulmonary bypass. J Cardiothorac Vasc Anesth 2004; 18:64–7
6. Engoren MC, Kraras C, Garzia F: Propofol-based *versus* fentanyl-isoflurane-based anesthesia for cardiac surgery. J Cardiothorac Vasc Anesth 1998; 12:177–81
7. Slogoff S, Keats AS: Randomized trial of primary anesthetic agents on outcome of coronary artery bypass operations. Anesthesiology 1989; 70:179–88
8. Cheng DC, Wall C, Djaiani G, Peragallo RA, Carroll J, Li C, Naylor D: Randomized assessment of resource use in fast-track cardiac surgery 1-year after hospital discharge. Anesthesiology 2003; 98:651–7
9. Cheng DC, Karski J, Peniston C, Asokumar B, Raveendran G, Carroll J, Nierenberg H, Roger S, Mickle D, Tong J, Zelovitsky J, David T, Sandler A: Morbidity outcome in early *versus* conventional tracheal extubation after coronary artery bypass grafting: A prospective randomized controlled trial. J Thorac Cardiovasc Surg 1996; 112:755–64
10. Cheng DC, Karski J, Peniston C, Raveendran G, Asokumar B, Carroll J, David T, Sandler A: Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. A prospective, randomized, controlled trial. Anesthesiology 1996; 85:1300–10
11. Dumas A, Dupuis GH, Searle N, Cartier R: Early *versus* late extubation after coronary artery bypass grafting: Effects on cognitive function. J Cardiothorac Vasc Anesth 1999; 13:130–5
12. Quasha AL, Loeber N, Feeley TW, Ullyot DJ, Roizen MF: Postoperative respiratory care: A controlled trial of early and late extubation following coronary-artery bypass grafting. Anesthesiology 1980; 52:135–41
13. Nicholson DJ, Kowalski SE, Hamilton GA, Meyers MP, Serrette C, Duke PC: Postoperative pulmonary function in coronary artery bypass graft surgery patients undergoing early tracheal extubation: A comparison between short-term mechanical ventilation and early extubation. J Cardiothorac Vasc Anesth 2002; 16:27–31
14. Reyes A, Vega G, Blancas R, Morató B, Moreno JL, Torrecilla C, Cereijo E: Early *vs* conventional extubation after cardiac surgery with cardiopulmonary bypass. Chest 1997; 112:193–201
15. Myles PS, Hunt JO, Fletcher H, Watts J, Bain D, Silvers A, Buckland MR: Remifentanil, fentanyl, and cardiac surgery: A double-blinded, randomized, controlled trial of costs and outcomes. Anesth Analg 2002; 95:805–12
16. Myles PS, Buckland MR, Weeks AM, Bujor MA, McRae R, Langley M, Moloney JT, Hunt JO, Davis BB: Hemodynamic effects, myocardial ischemia, and timing of tracheal extubation with propofol-based anesthesia for cardiac surgery. Anesth Analg 1997; 84:12–9
17. Silbert BS, Scott DA, Evered LA, Lewis MS, Kalpokas M, Maruff P, Myles PS, Jamrozik K: A comparison of the effect of high- and low-dose fentanyl on the incidence of postoperative cognitive dysfunction after coronary artery bypass surgery in the elderly. Anesthesiology 2006; 104:1137–45
18. Silbert BS, Santamaria JD, O'Brien JL, Blyth CM, Kelly WJ, Molnar RR: Early extubation following coronary artery bypass surgery: A prospective randomized controlled trial. Chest 1998; 113:1481–8
19. Berry PD, Thomas SD, Mahon SP, Jackson M, Fox MA, Fabri B, Weir WI, Russell GN: Myocardial ischaemia after coronary artery bypass grafting: Early *vs* late extubation. Br J Anaesth 1998; 80:20–5
20. van Mastrigt GA, Heijmans J, Severens JL, Fransen EJ, Roekaerts P, Voss G, Maessen JG: Short-stay intensive care after coronary artery bypass surgery: Randomized clinical trial on safety and cost-effectiveness. Crit Care Med 2006; 34:65–75
21. Michalopoulos A, Nikolaides A, Antzaka C, Deliyanni M, Smirli A, Geroulanos S, Papadimitriou L: Change in anaesthesia practice and postoperative sedation shortens ICU and hospital length of stay following coronary artery bypass surgery. Respir Med 1998; 92:1066–70
22. Maddali MM, Kurian E, Fahr J: Extubation time, hemodynamic stability, and postoperative pain control in patients undergoing coronary artery bypass surgery: An evaluation of fentanyl, remifentanil, and nonsteroidal antiinflammatory drugs with propofol for perioperative and postoperative management. J Clin Anesth 2006; 18:605–10
23. Kadoi Y, Saito S, Kunimoto F, Goto F, Fujita N: Comparative effects of propofol *versus* fentanyl on cerebral oxygenation state during normothermic cardiopulmonary bypass and postoperative cognitive dysfunction. Ann Thorac Surg 2003; 75:840–6
24. Bell J, Sartain J, Wilkinson GA, Sherry KM: Propofol and fentanyl anaesthesia for patients with low cardiac output state undergoing cardiac surgery: Comparison with high-dose fentanyl anaesthesia. Br J Anaesth 1994; 73:162–6
25. Esteban A, Alía I, Gordo F, Fernández R, Solsona JF, Vallverdú I, Macías S, Allegue JM, Blanco J, Carriedo D, León M, de la Cal MA, Taboada F, Gonzalez de Velasco J, Palazón E, Carrizosa F, Tomás R, Suarez J, Goldwasser RS: Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1997; 156(2 Pt 1):459–65
26. Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, Gasparetto A, Lemaire F: Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994; 150:896–903
27. Lellouche F, Mancebo J, Jolliet P, Roeseler J, Schortgen F, Dojat M, Cabello B, Bouadma L, Rodriguez P, Maggiore S, Reynaert M, Mersmann S, Brochard L: A multicenter randomized trial of computer-driven protocolized weaning from mechanical ventilation. Am J Respir Crit Care Med 2006; 174:894–900
28. Rose L, Presneill JJ, Johnston L, Cade JF: A randomised, controlled trial of conventional *versus* automated weaning from mechanical ventilation using SmartCare/PS. Intensive Care Med 2008; 34:1788–95
29. Rose L, Schultz MJ, Cardwell CR, Jouvet P, McAuley DF, Blackwood B: Automated *versus* non-automated weaning for reducing the duration of mechanical ventilation for critically ill adults and children. Cochrane Database Syst Rev 2013; 6:CD009235
30. Dongelmans DA, Veelo DP, Paulus F, de Mol BA, Korevaar JC, Kudoga A, Middelhoek P, Binnekade JM, Schultz MJ: Weaning automation with adaptive support ventilation: A randomized controlled trial in cardiothoracic surgery patients. Anesth Analg 2009; 108:565–71