Journal of Critical Care 33 (2016) 163–168

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

A randomized controlled trial of 2 protocols for weaning cardiac surgical patients receiving adaptive support ventilation☆,☆☆

M.K.P. Tam, MBBS [a], W.T. Wong, MBBS [b], C.D. Gomersall, MBBS [b,*], Q. Tian, PhD [b], S.K. Ng, MBBS [a], C.C.H. Leung, MBChB [b], M.J. Underwood, MD [c]

[a] Department of Anaesthesia & Intensive Care, Prince of Wales Hospital, Shatin, Hong Kong
[b] Department of Anaesthesia & Intensive Care, The Chinese University of Hong Kong, Shatin, Hong Kong
[c] Division of Cardiothoracic Surgery, Department of Surgery, The Chinese University of Hong Kong, Shatin, Hong Kong

ARTICLE INFO

Keywords:
Respiration, Artificial
Ventilator weaning
Coronary artery bypass
Adult
Critical care
Morbidity

ABSTRACT

Purpose: This study aims to compare the effectiveness of weaning with adaptive support ventilation (ASV) incorporating progressively reduced or constant target minute ventilation in the protocol in postoperative care after cardiac surgery.
Material and methods: A randomized controlled unblinded study of 52 patients after elective coronary artery bypass surgery was carried out to determine whether a protocol incorporating a decremental target minute ventilation (DTMV) results in more rapid weaning of patients ventilated in ASV mode compared to a protocol incorporating a constant target minute ventilation.
Results: Median duration of mechanical ventilation (145 vs 309 minutes; $P = .001$) and intubation (225 vs 423 minutes; $P = .005$) were significantly shorter in the DTMV group. There was no difference in adverse effects (42% vs 46%) or mortality (0% vs 0%) between the 2 groups.
Conclusions: Use of a DTMV protocol for postoperative ventilation of cardiac surgical patients in ASV mode results in a shorter duration of ventilation and intubation without evidence of increased risk of adverse effects.

1. Introduction

Rapid weaning and extubation are important components of "fast track" recovery after elective coronary artery bypass grafting [1-3]. Different strategies have been proposed to reduce the duration of mechanical ventilation including the use of microprocessor modes of ventilation such as adaptive support ventilation (ASV) [4,5]. This is a closed loop mode of ventilation whereby the inspiratory pressure and respiratory rate are automatically adjusted by a microprocessor to minimize the work of breathing. The optimal respiratory rate and tidal volume are determined from the Otis equation based on the expiratory time constant of the respiratory system. Pressure-controlled breaths are delivered when the patient is apneic; and pressure-assisted breaths, when the patient is making breathing efforts. The physician sets a target minute ventilation as a percentage of the predicted minute ventilation requirement (100 mL/min per kilogram of predicted body weight), and the ventilator adjusts the level of airway pressure delivered, to minimize the work of breathing. With increasing breathing effort, the pressure delivered to achieve the target minute ventilation will be decreased.

Adaptive support ventilation has previously been studied as a mode for weaning patients after cardiac surgery with studies suggesting it is superior to pressure regulated volume control with automode [6] and physician-directed weaning [7]. It is superior or equally efficacious to synchronized intermittent mandatory ventilation (SIMV) with pressure support (PS) [5,8] and equally efficacious to pressure control followed by PS [9]. However, the optimal protocol for weaning patients in ASV mode is unknown. Two studies have compared ASV with SIMV and PS. When the target minute ventilation was progressively reduced in the ASV group, Sulzer et al [5] demonstrated that ASV was associated with a shorter duration of mechanical ventilation. However, when the target minute ventilation was kept constant, the duration of mechanical ventilation was the same in the 2 groups [8]. This suggests that a protocol that incorporates a progressive reduction in target minute ventilation might reduce the duration of mechanical ventilation. Although this theory is not supported by the recent demonstration that ventilation and intubation time were equivalent regardless of whether target minute ventilation was adjusted [10], the protocol for reducing target minute ventilation in the more recent study was much less aggressive than in the study of Sulzer et al. The lowest target minute ventilation was 70%, whereas in the study of Sulzer et al, the lowest was 25%. We therefore hypothesized that a protocol incorporating a progressive aggressive

☆ Funding: The study was funded by departmental funds.
☆☆ Presented at the European Society of Intensive Care Medicine congress, Barcelona, 2014.
* Corresponding author at: Department of Anaesthesia & Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Ngan Shing Street, Shatin, Hong Kong.
E-mail address: gomersall@cuhk.edu.hk (C.D. Gomersall).

http://dx.doi.org/10.1016/j.jcrc.2016.01.018
0883-9441/

reduction in target minute ventilation would result in a reduction in duration of ventilation for patients who have undergone cardiac surgery when compared to a protocol incorporating a constant target minute ventilation (CTMV) and carried out a randomized controlled trial to test this hypothesis.

2. Materials and methods

The study was carried out in accordance with the Declaration of Helsinki and ICH-GCP. Approval to carry out the study was granted by the Joint Clinical Research Ethics Committee of the New Territories East Cluster and The Chinese University of Hong Kong. Written informed consent was obtained from all participants before study entry. Patients undergoing elective coronary artery bypass grafting by a single surgical team were screened for eligibility. Patients older than 18 years were considered eligible in the absence of exclusion criteria. Preenrollment exclusion criteria were concomitant valvular or aortic surgery, age older than 80 years, preoperative left ventricular ejection fraction less than 30%, chronic obstructive pulmonary disease requiring bronchodilator therapy, significant hepatic disease (alanine aminotransferase/aspartate aminotransferase >150 μ/L), and renal impairment (creatinine >200 μmol/L). Postenrollment exclusion criteria were severe early postoperative hemorrhage (chest tube drainage >500 mL/h), need for reoperation, myocardial ischemia (ST-segment depression) lasting more than 30 minutes, postoperative cardiac failure necessitating high-dose inotropes or intraaortic balloon pump, severe hypoxemia (ratio of arterial oxygen tension and fractional inspired oxygen <150 mm Hg) or new neurologic deficit.

The anesthetic and surgical approach was standardized. In brief, patients received their usual cardiac medications preoperatively and were premedicated with oral midazolam 0.1 to 0.2 mg/kg 1 hour before induction of anesthesia. Anesthesia was induced with a combination of intravenous (IV) fentanyl 2 to 10 μg/kg, IV midazolam 20 to 50 μg/kg, and sevoflurane (end-tidal concentration of 0.0%-6.0%). Muscle relaxation was achieved with IV rocuronium 1 mg/kg. Patients were intubated with an endotracheal tube with internal diameter of 7 mm for female or 8 mm for male patients. Anesthesia was maintained with a combination of IV propofol (0-8 mg/kg per hour), IV remifentanil 0 to 0.2 μg/kg per minute, and sevoflurane (end-tidal concentration 0.0%-4.0%) to keep bispectral index scale between 40 and 60. Boluses of IV fentanyl 50 to 100 μg were given as needed for intense stimulation (eg, sternal incision) and on rewarming. Muscle relaxation was maintained with intravenous infusion of atracurium 0.3 mg/kg per hour until closure of the sternum. For hemodynamic fluctuations unrelated to depth of anesthesia, IV phenylephrine 50 to 100 μg boluses, IV metoprolol 1 mg boluses, IV glyceryl trinitrate infusion, IV atropine, or fluid boluses were used according to the clinical situation. Coronary artery bypass grafting was performed by a single surgical team through a median sternotomy incision with saphenous vein or internal thoracic or radial arteries harvested as conduits. A dose of IV morphine 0.1 to 0.2 mg/kg was given before weaning off from cardiopulmonary bypass (CPB). Patients were kept sedated with IV propofol infusion at 1 to 2 mg/kg per hour until they were transferred to the intensive care unit (ICU).

In the ICU, all patients were ventilated using a Raphael ventilator with software version 3.19/3.1 (Hamilton Medical, Rhäzuns, Switzerland). Patients were randomized using a computer-generated sequence in sealed opaque envelopes to receive ASV according to 1 of 2 protocols during the postoperative period. Details of the protocols are given in Fig. 1. The protocols were identical in the initial controlled ventilation phase (phase 1) and the unassisted breathing trial (phase 3) but differed in the assisted breathing phase (phase 2). In ASV mode, the clinician set the target minute ventilation as a percentage of a standard value (100 mL/min per kilogram of predicted body weight). The decremental target minute ventilation (DTMV) protocol required bedside nurses to progressively reduce the target minute ventilation, whereas the target minute ventilation was maintained at 100% in the CTMV protocol. Immediately after arrival in the ICU, patients were ventilated according to their assigned protocol. Patients who were still ventilated by 8 hours were deemed protocol failures. They were assessed by the duty ICU medical staff and managed at their discretion. Patients who successfully completed a 30-minute unassisted breathing trial were extubated if duty medical staff determined that they met the following criteria: fully responsive, pain free, adequate cough, no significant hemorrhage (chest tube blood loss ≤100 mL/h), stable cardiorespiratory parameters (absence of uncontrolled arrhythmia, mean arterial pressure ≥60 mm Hg on dopamine <2 μg/kg per minute and/or epinephrine <0.1 μg/kg per minute, respiratory rate ≤30 breaths per minute), and satisfactory arterial blood gas results on a fractional inspired oxygen concentration less than or equal to 0.5 (pH 7.35-7.45, $Paco_2$ ≤50 mm Hg, Pao_2 ≥75 mm Hg).

Other aspects of postoperative care followed standard unit protocols including use of a heat and moisture exchange filter (Humid-Vent Filter Compact S; Teleflex Medical Sdn. Bhd., Kamunting, Malaysia). Arterial blood pressure, central venous pressure, electrocardiography, and pulse oximetry were monitored continuously. Normal saline and gelatin-based colloid solutions were used for fluid resuscitation. Hemoglobin concentrations were maintained at greater than or equal to 8 g/dL. Dopamine or epinephrine was used to maintain mean arterial pressure at greater than or equal to 60 mm Hg and glyceryl trinitrate and sodium nitroprusside to treat hypertension (mean arterial pressure ≥100 mm Hg). Bedside nurses assessed analgesic requirements and gave boluses of 1 to 2 mg morphine to a total of 10 mg on patient request if the patient was fully awake or if the patient was hypertensive and restless if still sedated from the residual effects of general anesthesia. No sedation was administered after admission to ICU.

The primary end point of the study was duration of postoperative ventilation. Secondary end points were duration of postoperative intubation, number of patients still ventilated at 8 hours, number of arterial blood gas samples, and number of manual ventilator setting changes. Other data collected are listed in Tables 1 to 4. Respiratory parameters were downloaded from the ventilator to a laptop running data capture software provided by the ventilator manufacturer. Hemodynamic data were recorded on a clinical information system (Drager Medical, Lubeck, Germany).

3. Statistical analysis

A prospective power calculation indicated that a sample size of 26 per group was required to achieve 80% power based on an effect size of a probability of 0.24 that an observation in the DTMV group is less than an observation in the CTMV group using the Mann-Whitney U test, an α of .05 (2 tailed), and assuming 6 patients in each group would drop out [11]. Duration of ventilation and intubation were analyzed using the Mann-Whitney U test. Other variables were tested for normality by assessing skewness and kurtosis. Hemodynamic and respiratory parameters and arterial blood gas results were analyzed using repeated measures analysis of variance (normally distributed data) or the Friedman test. Categorical data were analyzed using χ^2 or Fisher exact test as appropriate. $P < .05$ was considered significant. Statistical analysis was carried out using SPSS 14.0 for Windows (Chicago, IL).

4. Results

Of the 54 patients who were eligible for the study, 2 refused consent. Cardiorespiratory data for 1 patient were lost; otherwise, all data for the 52 patients enrolled in the study were analyzed (Fig. 2). The demographics of the 2 groups were not significantly different (Table 1).

In the CTMV group, 5 patients (19%) were ventilated for more than 8 hours but still failed to fulfill the criteria for an unassisted breathing trial, due to high $Paco_2$ (2 patients) and high inspiratory pressure (remaining 3 patients). After clinical assessment by the duty ICU physician, all underwent a successful unassisted breathing trial and were successfully