Efficacy of Cardiopulmonary Rehabilitation With Adaptive Servo-Ventilation in Patients Undergoing Off-Pump Coronary Artery Bypass Grafting

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Background: Postoperative complications after cardiac surgery increase mortality. This study aimed to evaluate the efficacy of cardiopulmonary rehabilitation with adaptive servo-ventilation (ASV) in patients undergoing off-pump coronary artery bypass grafting (OPCAB).

Methods and Results: A total of 66 patients undergoing OPCAB were enrolled and divided into 2 groups according to the use of ASV (ASV group, 30 patients; non-ASV group, 36 patients). During the perioperative period, all patients undertook cardiopulmonary rehabilitation. ASV was used from postoperative day (POD) 1 to POD5. Hemodynamics showed a different pattern in the 2 groups. Blood pressure (BP) on POD6 in the ASV group was significantly lower than that in the non-ASV group (systolic BP, 112.9±12.6 vs. 126.2±15.8 mmHg, P=0.0006; diastolic BP, 62.3±9.1 vs. 67.6±9.3 mmHg, P=0.0277). The incidence of postoperative atrial fibrillation (POAF) was lower in the ASV group than in the non-ASV group (10% vs. 33%, P=0.0377). The duration of oxygen inhalation in the ASV group was significantly shorter than that in the non-ASV group (5.1±2.2 vs. 7.6±6.0 days, P=0.0238). The duration of postoperative hospitalization was significantly shorter in the ASV group than in the non-ASV group (23.5±6.6 vs. 29.0±13.1 days, P=0.0392).

Conclusions: Cardiopulmonary rehabilitation with ASV after OPCAB reduces both POAF occurrence and the duration of hospitalization. (Circ J 2015; 79: 1290–1298)

Key Words: Adaptive servo-ventilation; Cardiopulmonary rehabilitation; Off-pump coronary artery bypass grafting

Off-pump coronary artery bypass grafting (OPCAB) is an established technique to achieve multivessel coronary artery revascularization, which tends to reduce the adverse effects of cardiopulmonary bypass (CPB). Although there are many conflicting reports, OPCAB has the potential to be associated with lower in-hospital mortality and complications, including stroke, acute renal failure, respiratory failure and infection, mediastinitis, cardiac failure, atrial fibrillation (AF), and bleeding-related events, compared with on-pump CPB. However, these reports also indicated that the incidence of complications with OPCAB was approximately 10%, and that respiratory failure or infection occurred in 3.7–5.9% of patients, which is significant. Recently, Fukui et al reported from a single-center study that the incidence of pneumonia after OPCAB was 1.5%, which although low, is nevertheless evidence that pneumonia remains one of the most serious complications related to mortality.

Pre- and postoperative cardiopulmonary rehabilitation in patients undergoing coronary artery bypass grafting (CABG) has reduced pulmonary complications, the incidence of AF, and the length of in-hospital stay after surgery. These results may be applied also to patients undergoing OPCAB, but further investigation is required to confirm this.

Pasquina et al conducted a systematic review, and reported that respiratory rehabilitation programs after cardiac surgery, which included respiratory physiotherapy, early mobilization, continuous positive airway pressure (CPAP), and incentive

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spirometry for promoting expectoration, were not effective in preventing respiratory complications. However, there have been several recent reports that respiratory rehabilitation with noninvasive positive pressure ventilation (NPPV) improved oxygenation and ventilation, reduced the work of breathing by inflating the alveoli, and increased cardiac output (CO) in the postoperative period by reducing left ventricular afterload.

Adaptive servo-ventilation (ASV), a novel NPPV therapy, was developed for Cheyne-Stokes respiration-central sleep apnea syndrome in patients with congestive heart failure (HF). This therapy synchronizes the flow pattern of the ventilator with the patient's own calculated respiratory flow pattern, and improves patient tolerability in comparison with other NPPV techniques. Recent studies showed that ASV improves the short-term prognosis in HF patients regardless of sleep-disordered breathing, and that cardiac function in both daytime and nighttime short-duration ASV users significantly improves. In addition, heart rate (HR) and blood pressure (BP) were significantly decreased, and CO significantly increased, within 30 min of the initiation of ASV in patients with chronic HF. These results suggest that ASV has the potential to improve cardiac and respiratory conditions in acute and chronic HF.

Therefore, we hypothesized that ASV would improve postoperative cardiac and respiratory conditions. The present study aimed to evaluate the efficacy of cardiopulmonary rehabilitation with ASV in patients undergoing off-pump CABG.

Methods

Subjects
From April 2010 to December 2013, isolated OPCAB was performed in 85 patients. To evaluate the usual rehabilitation programs, exclusion criteria were as follows: prior cardiac surgery; congestive HF; moderate-to-severe valvular disease requiring surgical intervention; prior implantation of a permanent pacemaker, implantable cardioverter defibrillator (ICD) or ICD with cardiac resynchronization therapy; history of chronic or paroxysmal AF; use of class I or III antiarrhythmic drugs; and refusal to participate in the rehabilitation program. After 19 patients had been excluded, 66 patients were enrolled in the study. All underwent cardiac rehabilitation during the perioperative period in the Department of Rehabilitation. All analyses were based on a retrospective review of medical records. The study was approved by the Ethics Committee of Hiroshima University. Informed consent for permission to use medical records for the purpose of research was given by all patients before the operation. All patients except one who refused to ASV were randomly assigned to 2 groups according to the use of ASV. All 30 patients of the ASV group completed the rehabilitation program through the perioperative period without any drop outs.

Study Protocol and Assessment of Hemodynamics
This study had 2 protocols: (1) comparison of just before and after ASV attachment to investigate the acute effect of ASV; and (2) comparison of the ASV and non-ASV groups to investigate the efficacy of using ASV. Preoperative characteristics (comorbidities, medications, echocardiographic findings, and laboratory data), operative data, and postoperative results were collected from medical records and compared between groups. For the assessment of hemodynamics, BP and HR at rest were averaged on each day from postoperative day (POD) 1 to POD10. However, BP and HR before and after ASV were measured separately to assess the acute effect of ASV.

Surgical Procedure and Postoperative Care
All preoperative cardiac medications, including β-blockers, calcium antagonists, angiotensin receptor blockers, and angiotensin-converting enzyme inhibitors, were continued until the day before surgery. The patients underwent OPCAB, which was performed using a standard surgical technique. General anesthesia was induced and maintained with remifentanil, propofol and rocuronium. Patients routinely received intravenous nitroglycerin (0.25–0.5 µg·kg⁻¹·min⁻¹) for the dilation of coronary arteries and the prevention of internal thoracic artery spasm. A median sternotomy was performed and all grafting materials, including the left internal thoracic artery, right internal thoracic artery, gastro-epiploic artery and saphenous vein, were harvested. Heparin (100IU/kg) was given, and the activated clotting time was maintained >300s. The distal anastomoses of grafts were performed using an Octopus II stabilizer (Medtronic, Inc, Minneapolis, MN, USA). Three deep pericardial retraction sutures were placed at the posterior fibrous pericardium, close to the left inferior pulmonary vein and inferior vena cava. The center between the left inferior pulmonary vein and the inferior vena cava was used as a lever to manipulate and rotate the heart into a vertical and lateral position along the stabilizer. Intracoronary shunts were used routinely for the left anterior descending artery and for all other patent arteries. Visualization was aided with a humidified carbon dioxide blower (Toyobo Co, Ltd, Osaka, Japan). The distal anastomoses were performed with a 7-0 or 8-0 polypropylene running suture. The proximal anastomoses were performed with a 6-0 polypropylene running suture using the Enclose II (Novare Surgical Systems, Inc, Cupertino, CA, USA) proximal suture device or partial aortic clamping. Protamine was used to reverse heparin anticoagulation. All patients were transferred to the intensive care unit under the care of anesthesiologists, and recovered from anesthesia on either the day of the operation or POD1.

For the prevention of arterial spasm, a continuous intravenous infusion of nitroglycerin (0.2–0.4 µg·kg⁻¹·min⁻¹) with/without diltiazem (0.5–1.0 µg·kg⁻¹·min⁻¹) was used intraoperatively, and during the first 24h after the operation. Anesthetic techniques and medications for the intraoperative and postoperative periods were similar in all patients. Low-dose aspirin was given to all patients following the procedure, and warfarin was used in addition to low-dose aspirin for patients with saphenous vein grafts. If necessary, inotropic drugs were used during the stay in the intensive care unit. During the study period, a cardiologist confirmed the diagnosis of AF and initiated prompt treatment using β-blockers, calcium antagonists, antiarrhythmic drugs and/or defibrillation. Oral cardiovascular agents, including β-blockers, long-acting calcium antagonists, angiotensin-converting enzyme inhibitors, and angiotensin-II receptor antagonists, were restarted on POD3 in patients who had received these agents preoperatively. Echo-cardiography was performed approximately 2 weeks after the operation.

Rehabilitation Program
A rehabilitation program was started ≥1 day preoperatively until discharge for all the study patients. The preoperative program included practice of breathing techniques and instruction in the use of the ASV system. In the early postoperative period (POD1–5), the rehabilitation program consisted of conventional perioperative exercises, including mobilization and respiratory training with or without ASV. On POD5, all patients were examined in their wards to determine if they could walk 100m. On the following POD (≥POD6), the rehabilitation program con-
Statistical Analysis

Data are presented as the mean±standard deviation. Continuous variables were compared between groups using Student’s t-test. Categorical variables were compared using a Chi-square test or Fisher’s exact test. Perioperative hemodynamic data were analyzed by repeated-measures analysis of variance with Fisher’s PLSD post hoc comparisons. All statistical analyses were performed using IBM SPSS Statistics version 21.0 software (IBM, USA). All P values <0.05 were considered significant.

Results

Preoperative Characteristics and Echocardiographic Data

The preoperative clinical characteristics of the patients are shown in Table 1. There were 50 male and 16 female patients with sisted of aerobic exercise using a treadmill or ergometer and muscle strength exercises. Oxygen administration was stopped when oxygen saturation was constant at >94% in room air. ASV was performed using an AutoSet CS® (ResMed, Sydney, NSW, Australia/Teijin Co, Tokyo, Japan) with the following pressure settings: end-expiratory pressure, 4 cmH2O; minimum pressure support, 3 cmH2O; and maximum pressure support, 10 cmH2O. After weaning from the ventilator, patients in the ASV group undertook conventional cardiopulmonary rehabilitation for 40 min, and then were attached to the ASV system for ≥30 min/day for 5 days after surgery. ASV was continued for a longer period if the patient wanted it or the physician judged it necessary. Patients were divided into 2 groups: a rehabilitation program using ASV (ASV group, n=30), and a rehabilitation program without ASV (non-ASV group, n=36).

Table 1. Characteristics of Patients Undergoing OPCAB and Cardiopulmonary Rehabilitation With ASV

|                          | Total (n=66) | ASV group (n=30) | Non-ASV group (n=36) | P value |
|--------------------------|-------------|------------------|----------------------|---------|
| Age (years)              | 69.4±9.8    | 71.0±8.4         | 68.1±10.7            | 0.2247  |
| Sex, male (%)            | 50 (76)     | 22 (73)          | 28 (78)              | 0.7760  |
| BMI (kg/m²)              | 24.0±3.7    | 23.9±3.6         | 24.1±3.8             | 0.7925  |
| Hypertension (%)         | 53 (80)     | 23 (77)          | 30 (83)              | 0.5467  |
| Hyperlipidemia (%)       | 43 (65)     | 23 (77)          | 20 (56)              | 0.1188  |
| Diabetes mellitus (%)    | 36 (55)     | 19 (63)          | 17 (47)              | 0.2218  |
| Renal insufficiency (creatinine >1.5 mg/dl) (%) | 5 (76) | 1 (3) | 4 (11) | 0.3663 |
| Hemodialysis (%)         | 3 (5)       | 0                | 3 (8)                | 0.2448  |
| Cerebrovascular disease (%) | 14 (21)     | 5 (17)           | 9 (25)               | 0.5484  |
| COPD (%)                 | 6 (9)       | 4 (13)           | 2 (6)                | 0.3989  |
| Smoking (%)              | 39 (59)     | 20 (67)          | 19 (53)              | 0.3180  |
| Preoperative medications |             |                  |                      |         |
| β-blocker (%)            | 32 (48)     | 14 (47)          | 18 (50)              | 0.8097  |
| ACEI/ARB (%)             | 35 (53)     | 12 (40)          | 23 (64)              | 0.0825  |
| Ca channel antagonist (%)| 30 (45)     | 15 (50)          | 15 (42)              | 0.6232  |
| Statin (%)               | 44 (67)     | 23 (77)          | 21 (58)              | 0.1893  |
| Coronary lesions         |             |                  |                      |         |
| Isolated left main trunk (%) | 1 (2)       | 0                | 1 (3)                |         |
| 1-vessel disease (%)     | 4 (6)       | 2 (7)            | 2 (6)                |         |
| 2-vessel disease (%)     | 17 (26)     | 8 (27)           | 9 (25)               |         |
| 3-vessel disease (%)     | 44 (67)     | 20 (67)          | 24 (67)              | 0.8292  |
| Echocardiographic data   |             |                  |                      |         |
| LA dimension (mm)        | 37.7±5.6    | 38.9±5.2         | 36.8±5.8             | 0.1520  |
| LVDd (mm)                | 48.5±5.5    | 48.4±4.8         | 48.6±6.1             | 0.8611  |
| LVDs (mm)                | 34.2±7.2    | 33.3±6.5         | 34.9±7.7             | 0.3693  |
| LA volume (ml)           | 58.0±16.7   | 58.1±13.4        | 58.0±19.3            | 0.9700  |
| LAVI (ml/m²)             | 34.7±11.6   | 36.3±8.7         | 33.3±13.4            | 0.3081  |
| LV ejection fraction (%) | 56.5±10.7   | 58.1±9.4         | 55.2±11.6            | 0.2891  |
| LVEDV (ml)               | 96.9±33.9   | 94.2±30.3        | 99.4±37.3            | 0.5774  |
| LVESV (ml)               | 45.2±27.5   | 42.3±25.2        | 47.9±29.8            | 0.4691  |
| PA-TDI duration (ms)     | 134.5±18.6  | 135.1±17.3       | 134.0±19.8           | 0.8090  |
| MR                       |             |                  |                      |         |
| None                     | 8 (28)      |                  | 9 (25)               |         |
| Trivial                  | 7 (24)      |                  | 13 (36)              |         |
| Mild                     | 14 (48)     |                  | 14 (39)              | 0.5718  |

Data are shown as the number of patients or mean±standard deviation. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor antagonist; ASV, adaptive servo-ventilation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; IVS, interventricular septum; LA, left atrial; LAVI, LA volume index; LV, left ventricular; LVDd, LV end-diastolic dimension; LVDs, LV end-systolic dimension; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume; OPCAB, off-pump coronary artery bypass grafting; PW, posterior wall.
Efficacy of Rehabilitation With ASV After OPCAB

Perioperative Hemodynamic Changes and Postoperative Results

Figure 1 shows changes in hemodynamics during rehabilitation with ASV. ASV was attached to the patient when hemodynamics were restored to the same level as before rehabilitation. The acute effect of ASV was investigated in the ASV group. HR was significantly decreased after >30 min after rehabilitation with ASV, however, no significant differences were observed for blood pressure (BP).

Intraoperative Factors

The perioperative factors are shown in Table 2. There were no significant differences between the groups in operative time, loss of blood or the number of distal anastomoses. Intraoperative medications, except for nicardipine (a calcium-channel blocker used to control hypertension during the operation), did not differ between the groups. Nicardipine was used more frequently in the non-ASV group than in the ASV group (P=0.0028).

Table 2. Intraoperative Factors of Patients Undergoing OPCAB and Cardiopulmonary Rehabilitation With ASV

|                          | Total (n=66) | ASV group (n=30) | Non-ASV group (n=36) | P value |
|--------------------------|-------------|------------------|----------------------|---------|
| Operation time (min)     | 308.2±79.9  | 289±70           | 324±85               | 0.0711  |
| Loss of blood (ml)       | 1,347±743   | 1,344±773        | 1,348±728            | 0.9822  |
| Distal anastomosis (n)   | 3.1±1.0     | 3.1±0.9          | 3.2±1.1              | 0.6056  |
| Intraoperative medication|             |                  |                      |         |
| Dopamine (%)             | 61 (92)     | 28 (93)          | 33 (92)              | 0.9999  |
| Dobutamine (%)           | 8 (12)      | 2 (7)            | 6 (17)               | 0.2753  |
| Diltiazem (%)            | 56 (85)     | 26 (87)          | 30 (83)              | 0.7454  |
| Milislol (%)             | 66 (100)    | 30 (100)         | 36 (100)             |         |
| Carperitide (%)          | 8 (12)      | 5 (17)           | 3 (8)                | 0.4525  |
| Nicardipine (%)          | 29 (44)     | 7 (23)           | 22 (61)              | 0.0028  |
| Landiolol (%)            | 24 (36)     | 14 (47)          | 10 (28)              | 0.1305  |

Abbreviations as in Table 1.
Body weight (BW) increased in both groups by POD3. However, on the day after the ASV protocol was completed (POD6), BW in the ASV group was significantly lower on POD6 (62.6±8.4 vs. 60.9±8.4 kg, P=0.0045). The reduction of BW from preoperatively to POD6 was significantly greater in the ASV group than in the non-ASV group (change of BW, −0.6±2.4 vs. 0.7±2.6 kg, P=0.0450). The white blood cell count showed similar changes in both groups. It had normalized by POD6, at which time it was significantly lower than on POD3 (ASV group, 13,596±3,556 vs. 8,457±2,819/μl, P<0.0001; non-ASV group, 11,742±3,301 vs. 7,907±1,940/μl, P<0.0001). There were no significant differences between the groups in hemoglobin concentration during the postoperative time course. C-reactive protein (CRP) concentration reached its peak value on POD3, and gradually decreased to POD6 and POD10. Moreover, the CRP values on POD6 and POD10 were significantly lower in the ASV group than in the non-ASV group (POD6: 3.2±3.6 vs. 5.6±3.1 mg/dl, P=0.0061; POD10: 1.9±1.3 vs. 2.8±1.5 mg/dl, P=0.0105).

Postoperative echocardiographic findings showed no significant differences between groups. The duration of oxygen inhalation was significantly shorter in the ASV group than in the non-ASV group (5.1±2.2 vs. 7.6±6.0 days, P=0.0238). The number of patients who accomplished the 100-m walk on POD5 was greater in the ASV group (21/30) than in the non-ASV group (12/36, P=0.0061).

Table 3. Perioperative Factors of Patients Undergoing OPCAB and Cardiopulmonary Rehabilitation With ASV

|                | Total (n=66) | ASV group (n=30) | Non-ASV group (n=36) | P value |
|----------------|-------------|------------------|----------------------|---------|
| **SBP (mmHg)** |             |                  |                      |         |
| Preoperative   | 125.3±13.4  | 123.5±12.1       | 126.3±14.1           | 0.4195  |
| POD1           | 118.3±17.7  | 120.1±13.9       | 116.2±20.4           | 0.3976  |
| POD3           | 125.5±16.2  | 127.7±14.2       | 123.8±17.7           | 0.3275  |
| POD6           | 120.0±15.5  | 112.9±12.6       | 126.2±15.8           | 0.0006  |
| POD10          | 117.0±12.4  | 114.7±9.4        | 119.0±14.3           | 0.1690  |
| **DBP (mmHg)** |             |                  |                      |         |
| Preoperative   | 64.8±9.0    | 62.9±8.1         | 66.2±9.9             | 0.1668  |
| POD1           | 63.9±11.0   | 65.4±11.8        | 62.2±10.7            | 0.2808  |
| POD3           | 65.7±10.9   | 66.5±10.2        | 65.1±11.5            | 0.6015  |
| POD6           | 65.0±9.3    | 62.3±9.1         | 67.6±9.3             | 0.0277  |
| POD10          | 61.8±7.5    | 60.6±6.5         | 62.7±8.1             | 0.2672  |
| **HR (beats/min)** |          |                  |                      |         |
| Preoperative   | 68.5±9.5    | 63.4±8.0         | 72.0±9.6             | 0.0005  |
| POD1           | 85.7±9.5    | 82.8±7.6         | 88.1±10.4            | 0.0270  |
| POD3           | 84.9±14.6   | 82.8±11.3        | 86.6±16.9            | 0.2922  |
| POD6           | 84.6±11.4   | 81.8±11.4        | 86.8±10.9            | 0.0803  |
| POD10          | 81.0±10.7   | 79.9±11.5        | 81.9±10.0            | 0.4421  |
| **PCWP (mmHg)**|             |                  |                      |         |
| Preoperative   | 9.2±3.3     | 9.0±3.8          | 9.4±3.0              | 0.7191  |
| **CI (L·min⁻¹·m⁻²)** |        |                  |                      |         |
| POD1           | 2.3±0.3     | 2.2±0.3          | 2.3±0.3              | 0.2261  |
| POD2           | 2.5±0.4     | 2.4±0.4          | 2.5±0.4              | 0.1470  |
| **Body weight (kg)** |         |                  |                      |         |
| Preoperative   | 61.5±12.1   | 60.4±10.3        | 62.4±13.5            | 0.5213  |
| POD3           | 64.0±11.1   | 62.0±8.4         | 66.1±13.4            | 0.2114  |
| Δ (preope-POD3) | 1.2±2.2    | 0.6±2.0          | 1.8±2.3              | 0.0590  |
| POD6           | 62.6±11.7   | 60.9±8.4         | 65.5±12.7            | 0.0622  |
| Δ (preope-POD6) | 0.1±2.5     | −0.6±2.4         | 0.7±2.6              | 0.0450  |
| POD10          | 60.6±12.1   | 58.1±10.6        | 62.8±13.1            | 0.1214  |
| Δ (preope-POD10)| −0.5±4.9    | −0.3±6.6         | −0.6±2.6             | 0.8173  |

(Continued on the next page.)
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The mode of NPPV frequently used after cardiac surgery is classified as CPAP and bilevel positive airway pressure (BiPAP). CPAP delivers a static airway pressure maintained throughout both the inspiratory and expiratory cycles. BiPAP delivers CPAP coupled with support pressure during the inspiratory cycle. In patients undergoing CABG, postoperative lung capacity oxygenation and atelectasis in patients under BiPAP improved more than in those under CPAP. ASV is a novel ventilation mode of BiPAP, which automatically controls the inspiratory rise time, the I:E ratio respiratory rate, and minute ventilation through an algorithm that adjusts these parameters based on samples obtained from the patient’s prior breathing pattern. This self-learning type of algorithm provides a synchronized and stable respiratory pattern with smooth positive pressure. These features may account for the high tolerability of ASV in the present study.

Postoperative pulmonary complications, including atelectasis, pneumonia and re-intubation, are associated with increased rates of morbidity and mortality. Because thoracic drainage tubes are usually inserted when the internal thoracic arteries are used, and pleural effusion with or without atelectasis occurs in most cases, atelectasis was not evaluated in the present study. However, Jaaly et al reported that using BiPAP after CABG significantly reduced the incidence of atelectasis to 3%.

Discussion

This study demonstrated the efficacy of cardiopulmonary rehabilitation with ASV in patients undergoing OPCAB. ASV decreased the incidence of POAF and shortened the duration of postoperative hospital stay. The results indicated that this novel rehabilitation program, with an exercise load and respiratory assist to reduce the breathing workload, facilitated the progression of cardiopulmonary rehabilitation and enhanced its effect.

All patients except one were discharged from hospital without any respiratory complications. One patient in the non-ASV group required re-intubation, which was performed uneventfully. On POD2, she was extubated uneventfully with good circulatory and respiratory function. However, she considered that volume overload had worsened her respiratory function, and decided to re-intubate. Her subsequent clinical course was uneventful.

The overall incidence of POAF was 23% (15/66). The incidence of POAF was lower in the ASV group than in the non-ASV group (10% vs. 33%, P=0.0377). The duration of postoperative hospitalization was significantly shorter in the ASV group than in the non-ASV group (23.5±6.6 vs. 29.0±13.1 days, P=0.0392). All patients were discharged without any serious complications. There were no operative deaths at 30 days in either group.

### Table 1

|                | Total (n=66) | ASV group (n=30) | Non-ASV group (n=36) | P value |
|----------------|-------------|------------------|----------------------|---------|
| **WBC (/μl)**  |             |                  |                      |         |
| POD1           | 13,378±3,621| 14,281±3,808     | 12,624±3,378         | 0.0658  |
| POD3           | 12,585±3,518| 13,596±3,556     | 11,742±3,301         | 0.0320  |
| POD6           | 8,157±2,376 | 8,457±2,819      | 7,907±1,940          | 0.3534  |
| POD10          | 7,810±2,196 | 7,941±2,369      | 7,701±2,069          | 0.6620  |
| **Hb (g/dl)**  |             |                  |                      |         |
| POD1           | 10.5±1.1    | 10.5±1.3         | 10.6±1.4             | 0.9414  |
| POD3           | 10.4±1.3    | 10.3±1.1         | 10.5±1.4             | 0.3905  |
| POD6           | 11.3±1.5    | 11.3±1.3         | 11.3±1.6             | 0.9282  |
| POD10          | 11.2±1.3    | 11.1±1.2         | 11.2±1.5             | 0.7854  |
| **CRP (mg/dl)**|             |                  |                      |         |
| POD1           | 6.4±3.9     | 4.9±2.8          | 7.7±4.3              | 0.0046  |
| POD3           | 14.7±8.8    | 10.2±5.5         | 18.5±9.3             | <0.0001 |
| POD6           | 4.5±3.5     | 3.2±3.6          | 5.6±3.1              | 0.0061  |
| POD10          | 2.4±1.4     | 1.9±1.3          | 2.8±1.5              | 0.0105  |
| **Echocardiographic data** | | | | |
| LA dimension (mm) | 35.7±5.4 | 36.7±5.2 | 35.0±5.6 | 0.2014 |
| LVDd (mm)       | 46.3±5.6   | 45.3±5.2        | 47.1±5.8             | 0.2042  |
| LVDs (mm)       | 33.6±6.7   | 33.0±6.5        | 34.1±7.0             | 0.5057  |
| LAV (ml)        | 53.2±13.0  | 53.5±11.5       | 52.9±14.5            | 0.8819  |
| LV ejection fraction (%) | 55.8±10.1 | 55.3±9.9 | 56.2±10.4 | 0.7388 |
| LVEDV (ml)      | 85.5±27.2  | 81.6±25.4       | 88.8±28.7            | 0.3420  |
| LVESV (ml)      | 40.0±21.6  | 38.1±21.9       | 41.5±21.6            | 0.5794  |
| Re-intubation (%) | 1 (2)   | 0 (3)           | 1 (3)                | >0.9999 |
| POAF (%)        | 15 (23)    | 3 (10)          | 12 (33)              | 0.0377  |
| Duration of oxygen inhalation (days) | 6.5±4.8 | 5.1±2.2 | 7.6±6.0 | 0.0238 |
| 100-m ambulation on POD5 (%) | 33 (50) | 21 (70) | 12 (33) | 0.0061 |
| **Postoperative hospital stay (days)** | 26.5±11.0 | 23.5±6.6 | 29.0±13.1 | 0.0392 |

CI, cardiac index; DBP, diastolic blood pressure; Hb, hemoglobin; HR, heart rate; LAV, LA volume; POAF, postoperative atrial fibrillation; PCWP, pulmonary capillary wedge pressure; POD, postoperative day; SBP, systolic blood pressure; WBC, white blood cell. Other abbreviations as in Table 1.
compared with an incidence of 24% with conventional respiratory care.22

It is well known that POAF is influenced by multiple risk factors.23,24 The preoperative factors include age, hypertension and diabetes mellitus; the intraoperative factors include operative stress and atrial ischemia; and the postoperative factors include volume overload, increased cardiac afterload, and inflammation. These changes may affect the atrial structural substrate for POAF, and cause atrial extrasystoles and/or autonomic nerve imbalance, triggering electrophysiological disorders including atrial flutter and fibrillation.

There is good evidence that respiratory support improves the cardiac conditions that can lead to POAF. Extravascular lung water is related to cardiac volume load, and is increased after extubation of CABG patients.25 Increased extravascular lung water was prevented when BiPAP was used after extubation of CABG patients.26 CPAP reduces transmural pressure of the left ventricle, resulting in decreased cardiac afterload.27 The use of ASV for 30 min reduces peripheral vascular resistance and increased arterial compliance.19 Short-term application of CPAP of 10cmH₂O for 10 min reduced cardiac norepinephrine spillover and inhibited cardiac sympathetic nervous activity.28 Short-term application of ASV for 30 min reduced cardiac sympathetic neuron activity.29 In the present study, ASV was used from POD1 to POD5, the time period during which POAF frequently occurs. An important finding was that the incidence of POAF was decreased to 10% in the ASV group compared with 33% in the group without ASV use.

BP may decrease after the application of ASV. Haruki et al19 reported that the short-term application of ASV for 30 min decreased HR, BP and CO. However, at the end of the follow-up period, BP was not decreased compared with baseline, and CO had significantly increased in conjunction with a reduction of systemic vascular resistance. Hieda et al reported that application of ASV for 20 min immediately reduced HR and respiratory rate, and decreased pulmonary vascular resistance and systemic vascular resistance, which were associated with sympathetic nerve activity.30 In the present study, the protocol to investigate the acute effect of ASV revealed that HR was significantly decreased 30 min after rehabilitation with ASV; however, HR during the postoperative time course was similar between the ASV and non-ASV groups, which suggests that ASV may reduce cardiac sympathetic nerve activity by stimulating pulmonary stretch receptors because of the lung infla-
tion, but changes in HR were affected by surgical stress and other factors that overwhelmed the effect of ASV. The time course of BP changes was compared between the ASV and non-ASV groups. No significant differences were observed at POD3 compared with baseline, but systolic and diastolic BPs at POD6 were significantly lower in the ASV group than in the non-ASV group. At POD10, BP was at the same level in both groups, which may reflect the fact that increased sympathetic nerve activity after surgery normalized earlier in the ASV group than in the non-ASV group. Further investigation is required to determine the mechanisms underlying the hemodynamic effects of ASV.

Vargas et al reported that postoperative lung function on POD1 was reduced to one-third of that before the operation, but restored to 50% on POD5. Increased vascular permeability after surgery increases the amount of extravascular lung water after extubation. Extracellular fluid returns from the extravascular space to blood vessels in the refilling stage, and pulmonary edema and AF often occur, especially in patients with hypovolemia. In this stage, respiration often shows a shallow, rapid and unstable pattern, which can undermine cardiopulmonary rehabilitation during the first 5 PODs. Hoffmann et al reported that the short-term application of NPPV for 45 min improved CO and mixed venous oxygen saturation, and increased urine volume. Several studies have reported that the application of NPPV or ASV increases the CI.

Several studies have reported that the application of NPPV or ASV increases the CI. Yamaeda et al reported that in HF patients with a higher PCWP value, ASV increased the stroke volume index. However, the patients with lower PCWP values did not respond to ASV. The cut-off value of PCWP in this study was 12 mmHg. In the present study, the PCWP values were low. The CI in the ASV group increased after surgery, but was not significantly different from that in the non-ASV group. In this sense, the effect of ASV may have been less.

Oxygen therapy was withdrawn earlier in the ASV group. Hoffman et al reported that urine volume was increased by the application of NPPV, which may be related to withdrawal of oxygen therapy. Similarly, although there was no statistical correlation, BW in the ASV group decreased significantly earlier than in the non-ASV group, which might have been related to the improvement of oxygenation.

In the present study, the number of patients who achieved the 100-m walk on POD5 was greater in the ASV group than in the non-ASV group, which may be related to prolonged hospital stay in the non-ASV group. In the Guidelines for Rehabilitation in Patients with Cardiovascular Disease in Japan, accomplishing the 100-m walking exercise is used as an indication of achieving independent walking during the postoperative recovery period. The accomplishment of this exercise suggests that our cardiopulmonary rehabilitation program with ASV was effective in controlling hemodynamics and sympathetic nerve activity, and promoted earlier improvement of respiratory function after CABG.

Study Limitations
First, the number of patients was small. Second, there were few circulatory data for the early postoperative period using ASV, because the Swan-Ganz catheter was removed on POD2, and wound dressings covering the median incision and drainage tubes made it difficult for echocardiographic examination. However, a significant reduction in the incidence of POAF and the duration of hospital stay was demonstrated. We plan to extend the study in the future with a prospective evaluation of ASV.

Conclusions
Cardiopulmonary rehabilitation with ASV after OPCAB had beneficial hemodynamic effects and reduced the incidence of arrhythmia. This might result in earlier accomplishment of a 100-m walk, and a shorter duration of postoperative hospital stay. We believe that our rehabilitation program is efficacious and plan to apply it to another cardiothoracic pathology.

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