Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

ORIGINAL ARTICLE
Cardiac Rehabilitation

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).[1,2] 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.[1–8] 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%,[9] which although low, is nevertheless evidence that pneumonia remains one of the most serious complications related to mortality.

Editorial p 1204

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.[10] 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

Received October 3, 2014; revised manuscript received January 21, 2015; accepted February 2, 2015; released online March 13, 2015
Time for primary review: 26 days

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ISSN-1346-9843 doi:10.1253/circj.CJ-14-1078

spirometry for promoting expectoration, were not effective in preventing respiratory complications.[11] 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.[12–14]

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.[15] Recent studies showed that ASV improves the short-term prognosis in HF patients regardless of sleep-disordered breathing,[16] and that cardiac function in both daytime and nighttime short-duration ASV users significantly improves.[17] 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.[18,19] 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 remifentanyl, propofol and rocuronium. Patients routinely received intravenous nitroglycerine (0.25–0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) 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 (100 IU/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 $\mu g \cdot kg^{-1} \cdot min^{-1}$) with/without diltiazem (0.5–1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was used intraoperatively, and during the first 24 h 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. Echocardiography 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 100 m. On the following POD (≥POD6), the rehabilitation program con-

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.

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 cmH_2O; minimum pressure support, 3 cmH_2O; and maximum pressure support, 10 cmH_2O. 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).

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

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
Dobtamine (%)	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.

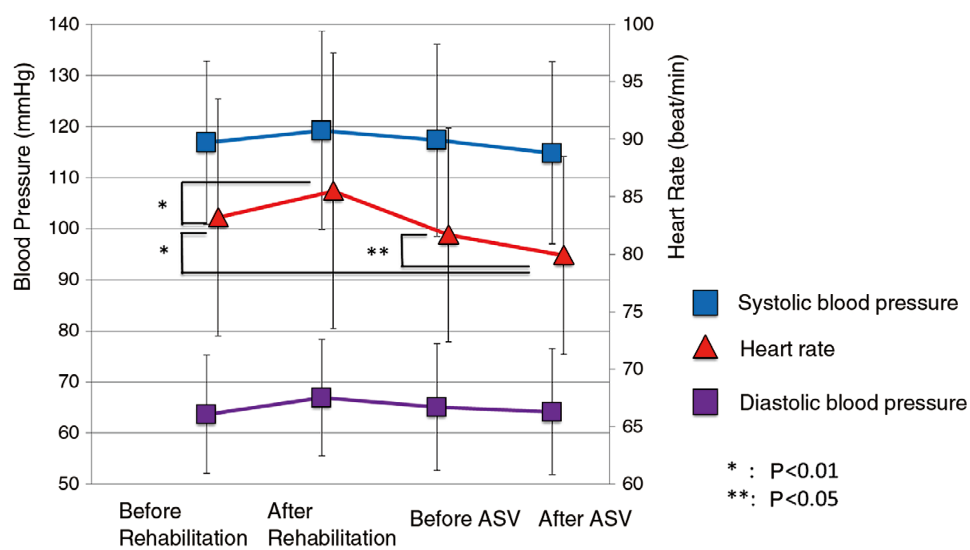

Figure 1. Time course of hemodynamics during cardiac rehabilitation with adaptive servo-ventilation (ASV). Heart rate significantly decreased after >30 min after rehabilitation with ASV, however, no significant differences were observed for blood pressure.

ages ranging from 34 to 89 years (mean age, 69.4±9.8 years). All patients had several coronary risk factors, including hypertension, hyperlipidemia, diabetes mellitus, and a past or current history of smoking. There were no significant differences between the groups with respect to preoperative characteristics and medications; 44 patients (67%) had 3-vessel disease, and there was no significant difference between the groups in this regard. No significant differences in the preoperative echocardiography data were found between groups, including the incidence of mitral valve regurgitation.

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).

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 of rehabilitation with ASV; however, no significant differences were observed for BP (HR, 81.7±9.3 vs. 79.9±8.6 beats/min, P=0.0376; systolic BP, 117.3±18.8 vs. 114.8±17.8 mmHg, P=0.2734; diastolic BP, 65.1±12.4 vs. 64.2±12.3 mmHg, P=0.5284).

Perioperative hemodynamics and postoperative results are shown in Table 3. BP changed similarly from before the operation to POD3. However, on the day after the ASV protocol was completed (POD6), BP in the ASV group was significantly decreased compared with POD3 (systolic BP, 112.9±12.6 vs. 127.7±14.2 mmHg, P=0.0036), and 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). On POD10, BP in the non-ASV group tended to decrease, and BP was similar in both groups (**Figure 2A**). The time course of changes in HR was similar in both groups. In all patients, HR significantly increased after the operation compared with baseline (85.7±9.5 vs. 68.5±9.9 beats/min, P<0.0001), remained elevated from POD1 to POD6, and had decreased slightly by POD10 (POD6, 84.6±11.4 vs. POD10, 81.0±10.7 beats/min, P=0.0071) (**Figure 2B**).

Preoperative pulmonary capillary wedge pressure (PCWP) was 9.2±3.3 mmHg in all cases and there was no significant difference between the groups. The cardiac index (CI) from POD1 through POD2 increased in both groups (ASV group, 2.2±0.3 vs. 2.4±0.4 $L \cdot min^{-1} \cdot m^{-2}$, P=0.0037; non-ASV group, 2.3±0.3 vs. 2.5±0.4 $L \cdot min^{-1} \cdot m^{-2}$, P=0.0007), and there was no significant difference between the groups.

Body weight (BW) increased in both groups by POD3. However, in the ASV group BW was significantly lower on POD6 than on POD3 (62.0±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±9.9	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 ($L \cdot min^{-1} \cdot m^{-2}$)				
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

(**Table 3** continued the next page.)

	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±1.4	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	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.

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 developed delirium and sudden respiratory distress at night. We 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.

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.

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.[20,21] In patients undergoing CABG, postoperative lung capacity oxygenation and atelectasis in patients under BiPAP improved more than in those under CPAP.[12,13] 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.[8] 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%

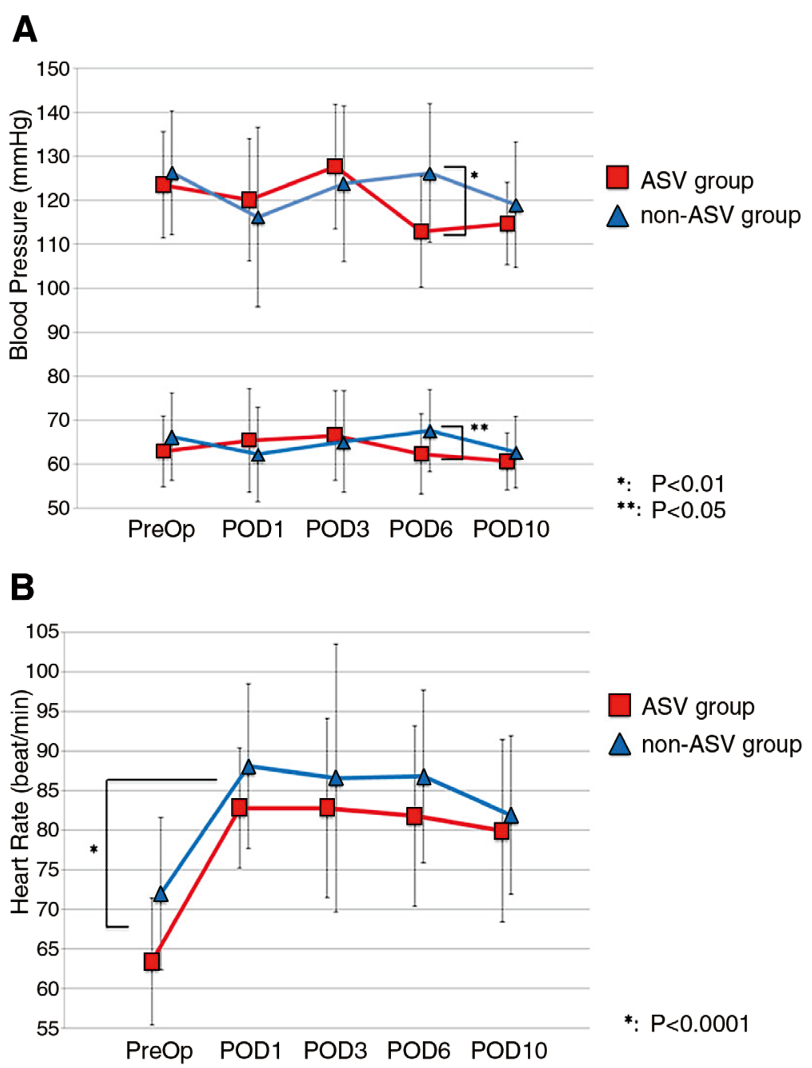

Figure 2. (**A**) Time course of blood pressure in the adaptive servo-ventilation (ASV) group compared with the non-ASV group. (**B**) Time course of heart rate, which increased on postoperative day (POD) 1, remained high from POD1 to 6, and then tended to decrease on POD10. There were no significant differences between the groups.

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 10 cmH_2O 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 al[19] 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 inflation, but changes in HR were affected by surgical stress and other factors that overwhelmed the effect of ASV.[31] 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.[32] Increased vascular permeability after surgery increases the amount of extravascular lung water after extubation.[25] 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 hypouresis. In this stage, respiration often shows a shallow, rapid and unstable pattern,[33] 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.[34] Borghi-Silva et al reported that isolated cardiopulmonary rehabilitation did not restore respiratory function by POD5, but that cardiopulmonary rehabilitation with positive end-expiratory pressure improved respiratory function other than vital capacity.[35]

Several studies have reported that the application of NPPV or ASV increases the CI.[18,19,34] Yamada et al[18] 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 that 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,[34] 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.

Acknowledgments

We gratefully acknowledge the advice from Professor Yasuki Kihara of the Department of Cardiovascular Medicine, Hiroshima University Hospital. We also thank members of the Heart Failure Center of Hiroshima University Hospital.

Disclosures

Conflict of Interest: The authors have no conflicts of interest to declare in this study. Name of grant: None.

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