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Original Article

Elimination of central sleep apnea by cardiac valve replacement: a continuous follow-up study in patients with rheumatic valvular heart disease

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ABSTRACT

Background: Recent studies have suggested that cardiac surgery may affect sleep-disordered breathing (SDB) in chronic heart failure patients. However, the dynamic changes in sleep apnea and heart function after cardiac surgery and the mechanisms responsible for these changes remain unknown.
Methods: Patients with rheumatic valvular heart disease (RVHD) and SDB were enrolled and followed up at three, six and 12 months after cardiac valve replacement (CVR). Baseline and follow-up clinical data consisting of NYHA classification, 6 min walk distance (6-MWD), medications, echocardiography, electrocardiography, chest X-ray, arterial blood gas, lung-to-finger circulation time (LFCT), and sleep data were collected and evaluated.
Results: Twenty-four central sleep apnea (CSA) patients and 15 obstructive sleep apnea (OSA) patients completed three follow-up assessments. Comparison of the baseline parameters between OSA patients and CSA patients showed that CSA patients had a worse baseline cardiac function assessed by higher NYHA class, shorter 6-MWD, larger left atrial diameter, longer LFCT, and enhanced chemosensitivity (higher pH and lower arterial carbon dioxide tension ($PaCO_2$)). A continuous significant elevation in 6-MWD and left ventricular ejection fraction and decrease in NYHA class, plasma BNP, and left atrial diameter were found in both CSA and OSA patients. When comparing CSA and OSA patients, the CSA indices were remarkably reduced at month 3 post CVR and sustained throughout the trial, whereas there were no significant decreases in OSA index and hypopnea index. pH values and LFCT were markedly decreased and $PaCO_2$ markedly increased in patients with CSA at the end of the third months following CVR. These changes were sustained until the end of the trial.
Conclusions: CSA patients with RVHD had a worse baseline cardiac function, enhanced chemosensitivity and disordered hemodynamic as compared with OSA patients with RVHD. CSA were eliminated after CVR; however, there were no changes in OSA. The elimination of CSA, post CVR, is associated with the combined efficacies of improvement of cardiac function, normalized chemosensitivity, and stabilized hemodynamic.

1. Introduction

Sleep-disordered breathing (SDB) may be classified into central sleep apnea (CSA) and obstructive sleep apnea (OSA). SDB, especially CSA, occurs frequently in patients with chronic heart failure (CHF). One large-scale study showed that SDB was present in 76% (40% CSA, 36% OSA) of patients with symptomatic CHF [1]. Of the two types of sleep apnea, studies have shown that OSA is implicated as a cardiovascular risk factor, and that CSA is an end-result of deteriorating cardiac function [2–5].

Several case reports strongly suggest that heart valve repair or replacement may lead to improvements in SDB [6–9]. Tomcsanyi and Yasuma reported that CSA events were substantially reduced after successful cardiac valve replacement (CVR) [7,9], and Collop

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and Mansfield found an improvement in CSA after successful heart transplant [10,11]. Abe [12] investigated 74 patients with valvular heart disease and reported significant improvements in CSA index (CSAI), pulmonary capillary wedge pressure (PCWP), and mean pulmonary artery pressure (PAP), and no changes in OSA index (OSAI) 14 days post heart-valve repair.

Although heart valve treatment has been reported to eliminate CSA or cause a shift from CSA to OSA, the mechanisms responsible for these effects are not fully understood. Some researchers [8,13–17] have suggested that the decrease in CSA may be related to enhanced lower partial pressure of arterial CO_2 ($PaCO_2$) and reduced lung-to-ear circulation time, whereas others [12] have considered that the improvements in CSA or shift from CSA to OSA may be the result of improved cardiac function.

In our previous study, we demonstrated that 38.8% of patients with rheumatic valvular heart disease (RVHD) also suffered from SDB [18]. We hypothesized that CVR surgery may affect CSA and OSA in patients with RVHD and SDB, and that the changes in SDB may be due to an improvement of heart function, chemosensitivity and hemodynamic circulation. In the current prospective study, we therefore investigated the dynamic changes in the various parameters at three, six, and 12 months after heart valve surgery in patients with RVHD and SDB.

2. Methods

2.1. Subjects and study design

Data were collected from 262 patients with RVHD who were admitted to the Cardiothoracic Surgery Department for CVR. The inclusion criteria were: (i) age 18–70 years; (ii) symptomatic stable heart failure, New York Heart Association (NYHA) class ⩾II despite optimal drug therapy; (iii) diagnosis of RVHD based on the 2004 World Health Organization (WHO) criteria for the diagnosis of rheumatic fever and rheumatic heart disease [19]; (iv) indications for valvular replacement surgery met the American College of Cardiology/American Heart Association (ACC/AHA) 2008 update guidelines for the management of patients with valvular heart disease [20]; and (v) patients combined with SDB (apnea–hypopnea index (AHI) ⩾10/h) according to the results of polysomnography (PSG).

The diagnosis of RVHD was based on the 2004 WHO criteria for the diagnosis of rheumatic fever and rheumatic heart disease [19]: a primary episode of rheumatic fever or a clinical rheumatic heart disease features currently, with typical rheumatic valvular lesions examined by Doppler echocardiography.

The indications for valvular replacement surgery were based on ACC/AHA 2008 update guidelines for the management of patients with valvular heart disease [20], including: (i) symptomatic patients with moderate to severe mitral stenosis or regurgitation; (ii) symptomatic patients with chronic moderate to severe aortic stenosis or regurgitation, and left ventricular systolic dysfunction (ejection fraction ⩽0.50) at rest; and (iii) decompensated heart failure with moderate to severe valvular lesions involved in at least two cardiac valves.

A PSG test was performed 1–7 (3.7 ± 1.6) days before CVR for each patient. According to the results of PSG, 70 patients were combined with SDB (48 patients with CSA (CSAI >50% AHI) and 22 patients with OSA (OSAI >50% AHI)). Of these, 39 patients (24 with CSA; 15 with OSA) successfully completed three follow-up assessments (three, six, and 12 months after CVR surgery) between April 2010 and January 2013.

This study was approved by the Institutional Patient Ethics Committee (IPEC approval #20092801) and registered on ClinicalTrials.gov (#NCT01426776). All patients gave written informed consent prior to study participation.

2.2. Baseline and follow-up assessments

Patients received optimal drug therapies (including digoxin, diuretics, nitrates, angiotensin-converting enzyme inhibitors, and β-blockers) to obtain a stable clinical status. Demographics and clinical data including age, sex, height, weight, body mass index (BMI), Epworth Sleepiness Scale (ESS) score, and medication use were prospectively entered into a dedicated database. All patients underwent standard clinical evaluations including New York Heart Association (NYHA) class, plasma brain natriuretic peptide (BNP), echocardiography, electrocardiography, arterial blood gas and lung-to-finger circulation time (LFCT). In addition, a 6 min walk distance (6-MWD) was performed within the first three days of hospital admission, according to American Thoracic Society guidelines [21]. 6-MWD was not performed in patients whose lower limb joints had been damaged by rheumatic fever.

Follow-up assessments of medications, BMI, blood pressure, NYHA class, plasma BNP, ESS score, echocardiography, electrocardiography, arterial blood gas, LFCT, 6-MWD, and sleep parameters were repeated three, six and, 12 months after CVR.

2.3. Polysomnography

The sleep study was performed by unattended overnight PSG (Embla S4500 System, Broomfield, CO, USA) as described previously [18]. Sleep was monitored using 5 electroencephalographic

Table 1
Baseline characteristics of the patients.

	CSA patients (n = 24)	OSA patients (n = 15)	t/χ^2	P
Age (years)	53.5 ± 8.9	51.4 ± 9.9	0.781	0.440
Sex			2.134	0.144
Male	12 (50.0)	11 (73.3)		
Female	12 (50.0)	4 (26.7)		
AF	20 (83.3)	4 (26.7)	12.945	0.000
BMI (kg/m^2)	22.8 ± 3.0	26.2 ± 4.3	2.972	0.005
6-MWT (m)	264.9 ± 77.4	320.9 ± 74.8	2.209	0.034
BNP (pg/mL)	605.6 ± 200.7	503.7 ± 103.5	2.058	0.047
ESS score	12.8 ± 5.8	11.5 ± 5.8	0.690	0.494
NYHA class			13.225	0.000
I	0 (0)	4 (26.7)		
II	8 (33.3)	9 (60.0)		
III	16 (66.7)	2 (13.3)		
Echocardiography				
LVEF (%)	58.8 ± 6.6	61.4 ± 6.3	1.200	0.238
LVDd (mm)	54.8 ± 10.0	55.4 ± 8.2	0.198	0.844
LVDs (mm)	37.7 ± 8.8	37.1 ± 7.2	0.222	0.825
LAD (mm)	55.4 ± 10.9	46.9 ± 13.5	2.158	0.038
PSG				
AHI (/h)	25.4 ± 13.0	21.5 ± 8.6	1.037	0.306
OSAI (/h)	3.3 ± 2.9	15.7 ± 7.0	7.715	0.000
CSAI (/h)	19.2 ± 10.0	2.2 ± 2.5	6.433	0.000
HI (/h)	2.9 ± 2.0	3.5 ± 2.6	0.848	0.402
Mean SpO_2 (%)	95.1 ± 1.4	95.6 ± 1.3	0.830	0.412
Minimal SpO_2 (%)	84.3 ± 5.8	81.1 ± 5.3	1.772	0.085
ODI (/h)	19.7 ± 16.4	12.7 ± 7.4	1.534	0.134
Sleep efficiency (%)	63.4 ± 7.4	67.1 ± 8.8	1.394	0.172
Awake arterial blood gases				
pH	7.447 ± 0.026	7.434 ± 0.034	1.315	0.197
PaO_2 (mmHg)	80.1 ± 13.7	81.2 ± 7.7	0.276	0.784
$PaCO_2$ (mmHg)	38.5 ± 5.3	43.7 ± 2.5	3.559	0.001
LFCT (s)	29.0 ± 6.7	18.5 ± 3.9	5.491	0.000

AF, atrial fibrillation; BMI, body mass index; 6-MWD, 6 min walk distance; NYHA, New York Heart Association; LVEF, left ventricle ejection fraction; LVDd, left ventricular diastolic dimension; LVDs, left ventricular systolic dimension; LAD, left atrial diameter; AHI, apnea/hypopnea index; CSAI, central sleep apnea index; OSAI, objective sleep apnea index; ESS, Epworth Sleepiness Scale; HI, hypopnea index; SpO_2, pulse oxygen saturation; ODI, oxygen desaturation index; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension.
Data are presented as no. (%) or mean ± SD.