IJC Heart & Vasculature 17 (2017) 23–29

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vasculature

Cardiac rehabilitation in patients with cardiovascular disease leads various hemodynamic parameters obtained using simple non-invasive tests to their appropriate levels

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ARTICLE INFO

Article history:
Received 6 July 2017
Received in revised form 28 September 2017
Accepted 2 October 2017
Available online xxxx

Keywords:
Comprehensive cardiac rehabilitation
Cardiovascular disease
Simple non-invasive tests
Arterial velocity pulse index
Cardiac index
Coefficient of variation of the R-R interval

ABSTRACT

We evaluated whether comprehensive cardiac rehabilitation (CR) in patients with cardiovascular disease (CVD) could improve various hemodynamic parameters obtained using simple non-invasive tests. We analyzed 48 CVD patients with (n = 38, CR group) or without (n = 10, non-CR group) a CR program, and prospectively followed them for 12 months. Various parameters were measured at baseline and after 12 months using 3 simple non-invasive tests: blood pressure (BP) and severity of atherosclerosis [arterial velocity pulse index (AVI) and atrial pressure volume index] were determined using PASESA®, an index of total autonomic nerve activity and a coefficient of variation of the R-R interval (CVRR) were determined using eHEART®, and the total peripheral resistance, stroke volume and cardiac index (CI) were determined using nico®. The main hemodynamic parameters did not change between baseline and 12 months in both groups. Patients in the CR group were divided into higher (H-) and lower (L-) systolic BP (SBP) or AVI according to the average value of SBP or AVI at baseline in the CR group. Patients with H-SBP or H-AVI in the CR group showed a significant reduction of SBP or AVI at 12 months. In addition, patients in the CR group were divided into H- and L- CI or CVRR according to the average value of CI or CVRR at baseline in the CR group. Patients with L-CI or L-CVRR in the CR group significantly improved after 12 months. In conclusion, CR may lead various hemodynamic parameters obtained using simple non-invasive tests to their appropriate levels.

1. Introduction

Comprehensive cardiac rehabilitation (CR) has been shown to improve cardiac function and prognosis in patients with cardiovascular disease (CVD) [1,2]. Recently, we reported that a 3-month CR program significantly decreased blood pressure (BP) [3] and improved atherosclerosis and sympathetic nerve as assessed by 3 simple non-invasive tests: BP and severity of atherosclerosis [arterial velocity pulse index (AVI) and arterial pressure volume index (API)] were determined using PASESA® (AVE-1500, Shisei Datum, Tokyo, Japan), an index of total autonomic nerve activity and a coefficient of variation of the R-R interval (CVRR) were determined using eHEART® (Parama-Tec, Fukuoka, Japan), and absolute and relative differences in BP between arms, pressure rate product (PRP), mean total peripheral resistance index (TPR), stroke volume (SV), and cardiac index (CI) were determined using nico® (Parama-Tec, Fukuoka, Japan) [4]. These 3 easy-to-use devices, PASESA® [5], nico PS-501® (North Parama Inc., Tokyo, Japan) [6] and eHEART® [7], are currently available for clinical use in Japan. We concluded that these simple non-invasive devices may be useful for assessing the effectiveness of CR. In addition, since we followed the patients for only 3 months [4], we considered a longer follow-up period (12 months) in this study. Therefore, we evaluated whether 12 months of comprehensive CR improved various hemodynamic parameters obtained using simple non-invasive tests in patients with CVD.

2. Methods

2.1. Study population and protocol

We enrolled 38 CVD outpatients into a CR program (CR group) and prospectively followed them for 12 months. We compared them to

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https://doi.org/10.1016/j.ijcha.2017.10.001

10 age-, gender- and body mass index (BMI)-matched CVD patients without CR (non-CR group, standard pharmacological care and no regular exercise habits). This study was approved by the Independent Review Board of Fukuoka University Hospital (#14-3-07) and registered under UMIN000016668. All subjects gave their written informed consent to participate.

2.2. Exercise protocol

The CR group participated in a supervised exercise training program at the hospital's gym for 12 months, with an average of 8 times (4–12 times) a month. Briefly, exercise intensity was chosen at 50% of peak VO_2 according to a cardio pulmonary exercise test (CPX) or Borg's scale 11–13 during exercise. Each session lasted about 1 h and consisted of a warm-up exercise (10 min) followed by 30 min of cycling or walking at the indicated exercise intensity and 20 min of cooling down and stretching. BP and heart rate (HR) were measured at rest and at the end of exercise, and an electrocardiogram [Central Monitor (DS-5700) Fukuda Denshi Co. Ltd., Tokyo, Japan] and Borg's scale were recorded during exercise.

2.3. Data collection

Patient characteristics including age, gender, BMI, prevalence of hypertension (HTN), dyslipidemia (DL) and diabetes mellitus (DM) and medications were assessed at baseline. Patients who had a current systolic BP (SBP)/diastolic BP (DBP) ≥140/90 mm Hg or who were receiving antihypertensive therapy were considered to have HTN. DM was defined using the Japan Diabetes Society Criteria or if the patient was being treated with an oral hypoglycemic agent or insulin. Patients with low-density lipoprotein cholesterol ≥140 mg/dl, triglyceride ≥150 mg/dl, and/or high-density lipoprotein cholesterol <40 mg/dl, or who were receiving lipid-lowering therapy, were considered to have DL. Ischemic heart disease (IHD) was defined as lumen diameter stenosis >50% in at least 1 major coronary artery as determined by coronary angiography and as diagnosed by old myocardial infarction. Heart failure was assumed based on the medical history, including medications and cardiac function. Medications included β-blocker, calcium channel blocker (CCB), angiotensin II receptor blocker (ARB)/angiotensin converting enzyme inhibitor (ACE-I) and diuretic. Various parameters were obtained using PASESA® [5], nico PS-501® [6] and eHEART® [7] at baseline and after 12 months.

2.4. CPX

Patients underwent symptom-limited CPX using a cycle ergometer with respiratory gas exchange analysis at baseline. The testing consisted of an initial 2 min of rest, 1 min of warm-up at 0 W, and full exercise under a ramp protocol with increments of 10 W/min. Expired gas analysis was performed throughout testing on a breath-by-breath basis, and work rate at anaerobic threshold (AT), volume of oxygen uptake (VO_2) at AT, O_2 pulse at AT, peak VO_2, minimum ventilation (VE)/volume of exhaled carbon dioxide (VCO_2), VE vs. VCO_2 slope, peak Gas exchange data were collected.

2.5. Measurements of parameters of arterial stiffness using PASESA®

We wrapped a cuff around the left upper arm of sitting patients and measured the brachial BP oscillometrically using PASESA® after at least 5 min of rest [4,5]. AVI, API, SBP, DBP and HR were collected.

2.6. Evaluation of various hemodynamic parameters using nico PS-501®

We wrapped cuffs around both the right and left upper arms of sitting patients. The nico PS-501® is a noninvasive BP-monitoring device based on the Korotkoff sound method. The PS-501® measures BP at the upper arm between 30 and 280 mm Hg and HR between 30 and 180 beat/min. Inflation is performed by an automatic pump system and deflation is controlled by an automatic pressure-release valve. Bilateral brachial PRP, SV, CI, and mean TPR were analyzed by a nico PS-501® [4,6]. We calculated absolute (|rt. BP − lt. BP|) and relative (rt. BP − lt. BP) differences in SBP and DBP between arms. Mean TPR was calculated by average of rt. TPR and lt. TPR.

2.7. Measurement of HRV using eHEART®

Beat-to-beat HR data in the supine position were continuously recorded for 5 min using eHEART® after at least 5 min of rest. This equipment is convenient and both rapid and simple to use, and 5 min of recording was sufficient for an analysis. Five minutes has been shown to be sufficient for short-term HRV analysis [7]. In addition, Bigger recommended that high-frequency (HF) power should be based on at least 1 min of recording, while low-frequency (LF) power required at least 2.5 min [8]. Using eHEART®, we evaluated parameters of heart rate variability (HRV), such as CVRR, HF, LF, and the ratio of LF to HF (LF/HF) [4,9]. The fluctuations of R-R intervals were integrated on the HF band (0.15–0.40 Hz) and the LF band (0.05–0.15 Hz). HRV was expressed as the power of the LF and HF components and the LF/HF power ratio.

2.8. Statistics

Statistical analysis was performed using the using the statistical software R (version 3.3.2). Data are expressed as the mean ± standard deviation or number (%). Categorical and continuous variables were compared between the groups by a chi-square analysis and *t*-test, respectively. The Spearman Rank Correlation Coefficient was used to evaluate associations between the groups. A value of $p < 0.05$ was considered significant.

3. Results

3.1. Patient characteristics at baseline in the non-CR and CR groups

Table 1 shows the patient characteristics at baseline in the non-CR and CR groups. In the CR group, the percentages (%) of male, HTN, DM, DL, IHD and heart failure were 56%, 62%, 15%, 74%, 39% and 37%, respectively. There were no significant differences in patient characteristics except for % ARB/ACE-I between the groups. % ARB/ACE-I in the CR group was significantly higher than that in the non-CR group.

The work rate at AT, VO_2 at AT, and O_2 pulse at AT at baseline and after 1 year were 41 ± 12 (23–62) and 42 ± 10 (16–66) watts, 13.8 ± 2.1 and 13.6 ± 2.4 ml/kg/min, 9.0 ± 1.7 and 8.8 ± 1.9 ml/beats, respectively. In addition, the peak VO_2, minimum VE/VCO_2, VE vs. VCO_2 slope, and peak Gas exchange at baseline and after 1 year were 16.6 ± 3.2 and 17.3 ± 3.6 ml/kg/min, 32 ± 3.2 and 33 ± 3.7 L, 29 ± 3.6 and 30 ± 3.7, and 1.0 ± 0.1 and 1.0 ± 0.1, respectively. There were no significant changes in these parameters between baseline and after 1 year.

Next, the patients were divided into 2 groups according to the average work rate at AT at baseline: higher work rate at AT at baseline (H-work rate group) and lower work rate at AT at baseline (L-work rate group). The work rate at AT after 1 year (38 ± 7 watts) significantly improved compared to that at baseline (32 ± 7 watts) ($p = 0.01$) in the L-work rate group, but not in the H-work rate group.

3.2. Determination of various parameters including BP, PR and arterial stiffness using PASESA® in the non-CR and CR groups

There were no significant differences in parameters obtained using PASESA® at baseline between the non-CR and CR groups, as shown in