



The effects of cardiac rehabilitation on haemodynamic parameters measured by impedance cardiography in patients with coronary artery disease

Uticaj kardiovaskularne rehabilitacije na hemodinamski status bolesnika sa koronarnom bolešću srca procenjen korišćenjem kardiografske impedance

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Abstract

Background/Aim. Well-organized cardiovascular rehabilitation (CVR) reduces cardiovascular burden by influencing cardiovascular risk factors, improving the quality of life, and reducing mortality and hospital readmission. However, its effects on hemodynamic status are largely unknown. The aim of our study was to evaluate the influence of a three-week CVR program on hemodynamic status and to investigate if there is a correlation between physical strain tolerance and hemodynamic parameters measured by impedance cardiography (ICG) before and after the CVR program in patients with coronary artery disease (CAD). **Methods.** Fifty-two patients attended a three-week CVR program. At the beginning and the end of the rehabilitation program, laboratory tests, exercise stress tests (EST), and ICG measurements were taken. **Results.** Patients showed better strain tolerance on the second exercise stress test (EST2) by achieving a higher strain level ($Z = 2.315$; $p = 0.021$) and a longer duration of the test ($Z = 2.305$; $p = 0.021$). There was a strong positive correlation between the level of EST2 and cardiac output (CO) ($r = 0.538$; $p < 0.001$) and stroke volume (SV) ($r = 0.380$; $p = 0.017$) on

the second ICG (ICG2). Moreover, there was a strong negative correlation between EST2 level and systemic vascular resistance (SVR) ($r = -0.472$; $p = 0.002$) and SVR index (SSVRI) ($r = -0.407$; $p = 0.010$) on ICG2. There was a strong positive correlation between EST2 duration and CO ($r = 0.517$; $p = 0.001$) as well as between EST2 duration and SV ($r = 0.340$; $p = 0.034$), and a strong negative correlation between EST2 duration and SVR ($r = -0.504$; $p = 0.001$) as well as between EST2 duration and SVRI ($r = -0.448$; $p = 0.004$), according to ICG2. **Conclusion.** Our study showed that a well-designed CVR program can lead to better physical strain tolerance in patients with CAD. Furthermore, CVR led to a significant positive correlation between EST and CO as well as between EST and SV measured by ICG. On the other hand, there was a significant negative correlation between EST and vascular-related parameters according to ICG at the end of the CVR program.

Key words: cardiography, impedance; coronary artery disease; myocardial infarction; physical exertion; plethysmography, impedance; rehabilitation.

Apstrakt

Uvod/Cilj. Dobro organizovana kardiovaskularna rehabilitacija (KVR) smanjuje kardiovaskularno opterećenje uticajem na faktore rizika od kardiovaskularnih bolesti, poboljšavajući kvalitet života i smanjujući smrtnost i ponovni kardiovaskularni događaj. Međutim, njeni efekti na hemodinamski status bolesnika uglavnom su nepoznati. Cilj rada bio je da se proceni uticaj tronedeljnog programa KVR na hemodinamski status i da se istraži postojanje povezanosti između tolerancije fizičkog napora i hemodinamskih parametara merenih kardiografskom impedancijom (*impedance*

cardiography – ICG) pre i posle programa KVR kod bolesnika sa oboljenjem koronarnih arterija. **Metode.** Ukupno 52 bolesnika učestvovala su u tronedeljnog programu KVR. Na početku i na kraju programa rehabilitacije vršeni su laboratorijski testovi, testovi fizičkim opterećenjem (TFO) i ICG merenja. **Rezultati.** Bolesnici su pokazali bolju toleranciju fizičkog napora na drugom TFO (TFO2) dostižući viši nivo opterećenja ($Z = 2,315$; $p = 0,021$) i duže trajanje testa ($Z = 2,305$; $p = 0,021$). Postojala je jaka korelacija između nivoa drugog TFO i minutnog volumena (MV) ($r = 0,538$; $p < 0,001$) i udarnog volumena (UV) ($r = 0,380$; $p = 0,017$) na drugoj ICG (ICG2). Takođe, postojala je jaka negativna korelacija između

nivoa TFO2 i sistemskog vaskularnog otpora (SVO) ($r = -0,472$; $p = 0,002$) i indeksa SVO (SVOI) ($r = -0,407$; $p = 0,010$) na ICG2. Postojala je jaka pozitivna korelacija između dužine trajanja TFO2 i MV ($r = 0,517$; $p = 0,001$), kao i između dužine trajanja TFO2 i UV ($r = 0,340$; $p = 0,034$), i jaka negativna korelacija između trajanja TFO2 i SVO ($r = -0,504$; $p = 0,001$), kao i između trajanja TFO2 i SVOI ($r = -0,448$; $p = 0,004$) na ICG2. **Zaključak.** Naša studija je pokazala da dobro dizajniran program KVR može dovesti do poboljšanja tolerancije fizičkog napora kod bolesnika sa oboljenjem koronarnih arterija. Takođe,

KVR je dovela do pozitivne korelacije između TFO i MV kao i TFO i UV procenjenih primenom ICG. Sa druge strane, postojala je značajna negativna korelacija između TFO i vaskularne rezistencije procenjene korišćenjem ICG na kraju programa KVR.

Ključne reči:
kardiografija, impedansna; koronarna bolest; infarkt miokarda; napor, fizički; pletizmografija, impedansna; rehabilitacija.

Introduction

Cardiovascular rehabilitation (CVR) is of great importance in the secondary prevention of cardiovascular diseases (CVD). On the one hand, it promotes recovery from CVD, and on the other, it prevents future cardiovascular events¹. Well-organized CVR, which includes supervised physical training, education, social support, and lifestyle changes, reduces cardiovascular burden by influencing cardiovascular risk factors, improving the quality of life, and reducing mortality and hospital readmission²⁻⁴.

The influence of CVR on hemodynamic status has been a subject of numerous studies. It can reduce heart rate, blood pressure, and rate-blood pressure product values^{5,6}. On the other hand, it can increase arterial compliance, especially in patients with diabetes mellitus⁷. This is why all relevant guidelines consider CVR as an indispensable part of secondary prevention in patients with CVD^{8,9}.

Thoracic impedance or impedance cardiography (ICG) is a simple, non-invasive diagnostic method used for assessing hemodynamic status by monitoring electrical conductivity changes of the thorax¹⁰. It is usually used in patients with heart failure where it can accurately assess stroke volume (SV) and cardiac output (CO)¹¹⁻¹³. Other indications include pulmonary hypertension, congenital heart diseases, sleep apnea, arterial hypertension, etc.¹⁴⁻¹⁷.

Using ICG, we can assess CO, SV, systemic vascular resistance (SVR), thoracic fluid content, and many other parameters that can help us both with the CVD diagnostic algorithm and the therapeutic approach.

The aim of our study was to evaluate the influence of a three-week CVR program on hemodynamic status in patients with coronary artery disease (CAD). Furthermore, we tried to investigate whether there was a correlation between physical strain tolerance and ICG parameters before and after the CVR program. To our knowledge, this was the first study that has provided this kind of investigation so far.

Methods

Recruitment and patients

The study involved 52 patients referred to the Institute for Treatment and Rehabilitation "Niška Banja" for a three-week CVR program after surviving myocardial infarction

(MI), percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG). Patients with an artificial valve, implemented permanent pacemaker, reduced ejection fraction ($EF < 50\%$), significant unsolved stenotic lesions on coronary arteries (stenosis $\geq 70\%$), atrial fibrillation, ventricular arrhythmia, severe anemia, impaired physical or mental conditions were excluded from the study. Data about ejection fraction, valve disease, and other echocardiographic parameters were extracted from previous medical examinations done after MI/PCI/CABG and before study enrollment.

Study design

The three-week CVR program included supervised and personalized physical training that involved cardiovascular exercise training, bicycle riding, and walking. At the beginning and the end of the CVR program, laboratory tests, exercise stress tests (EST), and ICG measurements were taken.

The tests were done on the Treadmill track using the Bruce protocol. After the initial EST, all patients underwent regular aerobic physical training, which included aerobic exercises, bicycle riding, and walking for 45 min *per* session, two sessions on a daily basis. All patients attended physical training five times a week, three weeks in a row. The intensity of physical activity was limited to the submaximal physical capacity determined at the level when 70–80% of the maximum heart rate was reached on the initial EST.

Exercise stress test

ESTs were done on the treadmill (3017 Full Vision Drive, Newton, Kansas, USA) according to the Bruce protocol. Tests were limited by submaximal heart rate (calculated as 85% from the 220-age equation), symptoms like chest pain, dyspnea, fatigue, dizziness, etc., and electropathological changes on electrocardiogram (ECG), which included horizontal or down-sloping ST-segment depression ≥ 1 mm, complexed ventricular arrhythmia that involved couplets of ventricular premature beats or ventricular tachycardia, patient's request to stop the test, and hypertensive reaction which was defined as a sudden increase of systolic BP to values ≥ 220 mmHg, or decreased in systolic BP > 10 mmHg.

Impedance cardiography

Hemodynamic data were obtained noninvasively using CardioScreen® 2000 (Medis GmbH, Germany). All patients underwent ICG monitoring for 15 min. Measurements were done at the same time, approximately half an hour after morning medications and before breakfast. All measurements were done in a supine position after 15 min of rest. Blood pressure was measured every three minutes, and ICG analyzes were taken every five min. The last recorded values were taken for statistical analysis.

Statistical analysis

Statistical analysis was performed using SPSS for Windows (Version 20; SPSS, Chicago, IL, USA). Frequencies and percentages were used for the description of the patient's characteristics. Numerical data were expressed as mean \pm standard deviation (SD). The Kolmogorov-Smirnov test was used to test the normality of data. Statistical significance for nominal data was tested with the χ^2 test and, where appropriate, the Fisher exact test. The Student's *t*-test was used to assess the statistical significance of parametric continuous data, and Mann-Whitney *U*-test and Wilcoxon Signed Ranks Test were for nonparametric continuous variables. The Pearson's correlation was used to determine the correlation between variables. Statistical significance was set to a level of $p < 0.05$.

Results*Baseline characteristics*

The study included 52 patients with CAD, 42 (80.8%) men and 10 (19.2%) women. The age structure was similar in both genders (male 56.62 ± 9.80 vs female 62.30 ± 9.08 ; $p = 0.101$). Thirty-nine (75%) patients suffered from arterial hypertension, 47 (90.4%) had lipid disorder or took lipid-lowering drugs, and 21 (40.4%) patients suffered from diabetes mellitus. Thirty-nine (75%) patients were smokers or ex-smokers, and 21 (40.4%) had a positive family anamnesis for CVD. Forty-four (84.6) patients survived MI, 35 (67.3%) underwent PCI, and 13 (25%) patients had CABG (Table 1).

Laboratory measurements

At the beginning and the end of CVR, laboratory parameters were measured (Table 2). Cholesterol, low-density lipoprotein (LDL), glycosylated hemoglobin (HbA1c), and creatinine kinase (CK) were lower at the end of CVR compared to the values at the beginning of CVR but without statistical significance. On the other hand, the values of erythrocytes ($t = 3.859$; $p < 0.001$), hemoglobin ($t = 3.245$; $p = 0.002$), and hematocrit ($t = 3.551$; $p = 0.001$) were significantly higher during the second measurement.

Table 1
Baseline characteristics of patients

Parameters	No	Yes
	n (%)	n (%)
Arterial hypertension	13 (25.0)	39 (75.0)
Hyperlipidemia	5 (9.6)	47 (90.4)
Diabetes mellitus	31 (59.6)	21 (40.4)
Smoking habit	13 (25.0)	39 (75.0)
Heredity	21(40.4)	31 (59.6)
Myocardial infarction	8 (15.4)	44 (84.6)
Coronary artery by-pass surgery	39 (75.0)	13 (25.0)
Percutaneous coronary intervention	17 (32.7)	35 (67.3)

Table 2
Laboratory measurements at the beginning and the end of rehabilitation

Parameters	At the beginning (mean \pm SD)	At the end (mean \pm SD)	t^*Z	p
Cholesterol	4.08 \pm 0.93	4.01 \pm 0.86	0.683	0.498
LDL	2.42 \pm 0.74	2.39 \pm 0.77	0.250	0.804
HDL	0.99 \pm 0.20	0.94 \pm 0.18	2.067	0.044
Triglyceride	1.59 \pm 0.72	1.59 \pm 0.64	0.770	0.939
Glucose	5.97 \pm 1.17	6.22 \pm 1.67	0.376*	0.707
HbA1c	5.42 \pm 1.42	5.28 \pm 1.47	1.374*	0.078
CK	157.60 \pm 109.27	142.60 \pm 78.77	1.167	0.250
CKMB	17.08 \pm 8.45	17.87 \pm 9.08	0.596*	0.551
Hematocrit	0.41 \pm 0.03	0.42 \pm 0.04	3.551	0.001
Erythrocytes	4.74 \pm 0.44	4.85 \pm 0.45	3.859	< 0.001
Hemoglobin	139.02 \pm 12.24	141.35 \pm 12.36	3.245	0.002
Creatinine	98.22 \pm 19.37	98.44 \pm 15.81	0.102	0.919
AUR	341.48 \pm 106.03	331.14 \pm 104.53	1.065	0.294

Z – Wilcoxon Signed Ranks Test; LDL – low-density lipoproteins; HDL – high-density lipoproteins; HbA1c – glycosylated hemoglobin; CK – creatinine kinase; MB – myocardial fraction; AUR – acidum uricum; SD – standard deviation.

Exercise stress test and impedance cardiography

Additionally, all patients underwent EST and ICG measurements at the beginning and the end of the CVR program (Table 3). Patients showed better strain tolerance on the second EST (EST2) by achieving a higher strain level ($Z = 2.315$; $p = 0.021$) and longer duration of the test ($Z = 2.305$; $p = 0.021$) compared to the values of the first EST (EST1). Furthermore, a higher number of patients achieved submaximal heart rate values on the EST2 ($Z = 3.153$; $p = 0.002$).

According to impedance cardiography, CO and SV were higher at the end of CVR, but without any statistical significance ($t = 0.512$; $p = 0.611$ and $Z = 1.349$; $p = 0.184$). On the other hand, heart rate, systemic vascular resistance index (SVRI), and stroke systemic vascular resistance index (SSVRI) were lower during the second measurement, but also without statistical significance ($Z = 1.068$; $p = 0.292$, $Z = 0.510$; $p = 0.613$ and $Z = 0.950$; $p = 0.348$).

Correlation between exercise stress test and impedance cardiography

There was no significant correlation between the levels of the EST1 and the parameters of the first ICG measurements (ICG1). On the other hand, there was a strong positive correlation between the levels of EST2 and CO ($r = 0.538$; $p < 0.001$) as well as between the levels of EST2 and SV ($r = 0.380$; $p = 0.017$), according to the second ICG measurements (ICG2). Moreover, there was a strong negative correlation between EST2 levels and SVR ($r = -0.472$; $p = 0.002$) as well as between EST2 levels and SVRI ($r = -0.407$; $p = 0.010$), measured by ICG2 (Table 4).

CO significantly positively ($r = 0.357$; $p = 0.026$) and SVR ($r = -0.409$; $p = 0.010$) and SVRI ($r = -0.356$; $p = 0.026$) significantly negatively correlated with EST1 duration when ICG1 parameters were compared. There was a strong positive correlation between EST2 duration and CO ($r = 0.517$; $p = 0.001$) as well as between EST2 duration and

Table 3**Exercise stress test and impedance cardiography**

Parameters	At the beginning (mean \pm SD)	At the end (mean \pm SD)	t^*/Z	p
Exercise stress test				
level	2.93 \pm 1.10	3.24 \pm 0.87	2.315*	0.021
duration (min)	7.13 \pm 3.30	7.79 \pm 2.63	2.305*	0.021
SHR (bpm)	0.43 \pm 0.50	0.70 \pm 0.46	3.153*	0.002
Impedance cardiography				
CO (L/min)	5.85 \pm 1.19	5.91 \pm 1.32	0.512	0.611
SV (mL)	90.91 \pm 22.91	93.63 \pm 22.69	1.349	0.184
ACI (1/100/s ²)	77.09 \pm 26.53	79.21 \pm 27.39	0.679	0.490
VI (1/1000/s)	47.07 \pm 15.04	47.84 \pm 14.19	0.499	0.620
BP systolic (mmHg)	127.77 \pm 9.54	128.77 \pm 12.94	0.453	0.666
BP diastolic (mmHg)	75.84 \pm 9.34	85.79 \pm 8.02	0.041	0.968
HR (bpm)	65.14 \pm 9.73	63.84 \pm 9.27	1.068	0.292
SVR (dyne·s/cm ⁵)	1237.93 \pm 275.98	1238.40 \pm 311.27	0.004	0.997
SVRI (dyne·s/cm ⁵ /m ²)	2397.40 \pm 450.33	2368.81 \pm 502.97	0.510	0.613
SSVRI (dyne·s/cm ⁵ /m ²)	156.95 \pm 34.58	152.91 \pm 36.40	0.950	0.348

Z – Wilcoxon Signed Ranks Test; SHR – submaximal heart rate; CO – cardiac output; SV – stroke volume; ACI – acceleration index; VI – velocity index; BP – blood pressure; HR – heart rate; SVR – systemic vascular resistance; SVRI – SVR index; SSVRI – stroke SVRI; SD – standard deviation.

Table 4**Correlation between the exercise stress test (EST) level and impedance cardiography (ICG) parameters**

ICG parameters	EST1 level		EST2 level	
	r	p	r	p
CO (L/min)	0.266	0.102	0.538	< 0.001
SV (mL)	0.177	0.280	0.380	0.017
ACI (1/100/s ²)	0.075	0.652	0.265	0.104
VI (1/1000/s)	0.172	0.295	0.284	0.079
BP systolic (mmHg)	0.078	0.635	0.128	0.438
BP diastolic (mmHg)	0.082	0.619	0.008	0.964
HR (bpm)	0.155	0.345	0.187	0.255
SVR (dyne·s/cm ⁵)	-0.209	0.201	-0.472	0.002
SVRI (dyne·s/cm ⁵ /m ²)	-0.163	0.322	-0.407	0.010
SSVRI (dyne·s/cm ⁵ /m ²)	-0.031	0.850	-0.236	0.148

For abbreviations see under Table 3.

SV ($r = 0.340$; $p = 0.034$), and a strong negative correlation between EST2 duration and SVR ($r = -0.504$; $p = 0.001$) as well as between EST2 duration and SVRI ($r = -0.448$; $p = 0.004$) measured by ICG2 (Table 5).

coronary heart disease (CHD) patients, CVR led to a better lipid profile (total cholesterol, triglycerides, LDL, and HDL). However, the CVR program in this study included 24 exercise sessions scheduled over eight weeks⁴¹.

Table 5
Correlation between exercise stress test (EST) duration and impedance cardiography (ICG) parameters

ICG parameters	EST1 duration (min)		EST2 duration (min)	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
CO (L/min)	0.357	0.026	0.517	0.001
SV (mL)	0.246	0.131	0.340	0.034
ACI (1/100/s ²)	0.170	0.302	0.226	0.167
VI (1/1000/s)	0.257	0.115	0.264	0.104
BP systolic (mmHg)	-0.075	0.649	0.061	0.714
BP diastolic (mmHg)	-0.040	0.807	-0.056	0.737
HR (bpm)	0.161	0.328	0.225	0.169
SVR (dyne·s/cm ⁵)	-0.409	0.010	-0.504	0.001
SVRI (dyne·s/cm ⁵ /m ²)	-0.356	0.026	-0.448	0.004
SSVRI (dyne·s/cm ⁵ /m ²)	-0.182	0.267	-0.246	0.131

For abbreviations see under Table 3.

Discussion

The beneficial effects of CVR are proven in patients with coronary artery disease, severe arterial hypertension, heart failure, heart valve repair, and heart transplantation¹⁸. A well-designed CVR program reduces cardiovascular mortality and hospital readmission and increases the quality of life in CVD patients^{19–21}. This is why relevant Guidelines give recommendations for CVR in patients with CVD^{8, 22–27}. Three main postulates of CVR are exercise training, lifestyle changes, and psychological intervention¹⁸. The main goal of CVR is “to provide the best possible physical, mental, and social conditions, so that the patients may, by their efforts, preserve or resume optimal functioning in their community and through improved health behavior slow or reverse the progression of the disease”²⁸.

Physical activity as a cornerstone of CVR has a positive effect on CVD regardless of patients' reduced or preserved ejection fraction^{8, 29}. In addition, the beneficial effects of exercise-based CVR do not depend on gender or age structure^{30, 31}. It increases physical strain tolerance³⁰ and arterial compliance⁷, improves lipid profile^{32, 33}, reduces the symptoms of depression^{34–36}, and leads to weight and blood pressure reduction^{37, 38}. It can even induce gray matter volume recovery³⁹. Our study once again showed that personalized and supervised physical training improves physical strain tolerance. The average strain level was higher, and the duration of the test was significantly longer in the second EST. Additionally, a higher number of patients achieved submaximal heart rate on EST2 compared to EST1.

On the other hand, CVR did not lead to significant changes in lipid profile or any other laboratory parameters except red blood count. It did reduce total cholesterol, LDL, and HbA1c, but without statistical significance. This is probably due to the shorter duration of the CVR program, as our study included patients with three-week CVR. For significant laboratory changes, CVR should last longer, at least eight weeks^{31, 32, 40}. For example, in a study with 547

Furthermore, Vergès et al.⁴² showed in their research that CVR could improve response to the hypolipidemic therapy in patients with CHD. However, the average duration of CVR in this study was two months. On the other hand, we noted an improvement in red blood count which can have a positive impact on functional capacity⁴³.

By using ICG, we tried to investigate the effects of CVR on hemodynamic status in CHD patients. Besides CO and SV, we assessed contractility-related (VI, ACI) and vascular system-related parameters (SVR, SVRI, SSVRI). It is well known that physical activity can decrease blood pressure values through the reduction of vascular resistance⁴⁴. The exact mechanism of how physical activity leads to vascular resistance reduction is unknown, but it probably includes the sympathetic nervous system and renin-angiotensin-aldosterone system⁴⁵. Furthermore, a combination of endurance and resistance training can improve endothelial function and arterial compliance^{46, 47}. In our study, exercise-based CVR did lead to SVRI and SSVRI reduction, but without statistical significance ($Z = 0.510$; $p = 0.613$ and $Z = 0.950$; $p = 0.348$). However, we emphasize the fact that the beneficial effects of exercise training are dose-dependent. It would be interesting to see whether the reduction of vascular-related parameters would be statistically significant if the CVR program lasted eight or twelve weeks.

Beneficial but temporary results of CVR on hemodynamic status are found in patients with stable chronic heart failure⁴⁸. Using ICG, Gielerak et al.⁴⁹ showed that CVR could reduce fluid retention in patients with HF. Moreover, exercise training can improve SV and CO⁵⁰. However, in our study, CO and SV were higher at the end of CVR, but without any statistical significance ($t = 0.512$; $p = 0.611$ and $Z = 1.349$; $p = 0.184$). Other studies that investigated the influence of physical training on SV or CO included patients with reduced ejection fraction or patients with heart failure with preserved EF (HFpEF). Our study included stable patients with preserved EF and without any symptoms and signs of HF.

The next step in our investigation was to assess whether there was a correlation between the parameters of the exercise stress test and ICG. There was no significant correlation between the average level of EST1 and ICG1 parameters. On the other hand, there was a strong positive correlation between the level of EST2 and CO ($r = 0.538$; $p < 0.001$) and between the level of EST2 and SV ($r = 0.380$; $p = 0.017$) according to ICG2. Moreover, there was a strong negative correlation between the EST2 level and SVR ($r = -0.472$; $p = 0.002$) as well as between the EST2 level and SVRI ($r = -0.407$; $p = 0.010$) according to ICG2. CO significantly positively ($r = 0.357$; $p = 0.026$) and SVR ($r = -0.409$; $p = 0.010$) and SVRI ($r = -0.356$; $p = 0.026$) significantly negatively correlated with EST1 duration when ICG1 parameters were compared. There was a strong positive correlation between EST2 duration and CO ($r = 0.517$; $p = 0.001$) as well as between EST2 duration and SV ($r = 0.340$; $p = 0.034$), and a strong negative correlation between EST2 duration and SVR ($r = -0.504$; $p = 0.001$) as well as between EST2 duration and SVRI ($r = -0.448$; $p = 0.004$) according to ICG2.

These results show that CVR has a great influence on hemodynamic parameters. Namely, CVR led to a positive correlation between physical strain tolerance and cardiac and stroke volume and a better negative correlation between physical strain tolerance and peripheral vascular resistance. As far as we know, this is the first study that investigated the effects of CVR on hemodynamic parameters and its correlation with physical strain tolerance in patients with CAD and preserved ejection fraction. An implementation of ICG as a valuable tool in assessing the effects of CVR on the

hemodynamic status of CAD patients should be considered.

Study limitations

There are several limitations to this study: 1) the study sample was relatively small. However, almost all studies that involved ICG as a diagnostic tool included 50 patients or less; 2) we did not perform echocardiographic examinations. It would be interesting to see how some ICG parameters (*i.e.*, SV and CO) correlate with some echocardiographic parameters (*i.e.*, left ventricular mass index and cardiac index); 3) our study included the CVR program that lasted for three weeks. We consider that a longer CVR duration (*i.e.*, eight weeks) could have greater beneficial effects on the hemodynamic status of CHD patients.

Conclusion

Our study once again showed that a well-designed CVR program could lead to better physical strain tolerance in patients with CAD. Furthermore, CVR led to a significant positive correlation between EST and cardiac output as well as between EST and stroke volume measured by ICG. On the other hand, there was a significant negative correlation between EST and vascular-related parameters according to ICG at the end of the CVR program.

Conflict of interests

The authors have no conflict of interest to declare regarding the present paper.

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