General Cardiology

CARDIOLOGY

Cardiology 1996;87:271–275

William E. Lawson
John C.K. Hui
Zhen Sheng Zheng
Lynn Burger
Lixin Jiang
Oneida Lillis
Zvi Oster
Harry Soroff
Peter F. Cohn

Departments of Medicine, Surgery and Radiology, SUNY Health Sciences Center, Stony Brook, N.Y., USA

Improved Exercise Tolerance following Enhanced External Counterpulsation: Cardiac or Peripheral Effect?

Key Words
Counterpulsation
Coronary disease
Exercise tolerance

Abstract
The effect of treatment with enhanced external counterpulsation (EECP) on exercise hemodynamics and myocardial stress perfusion in 27 patients with chronic stable angina was studied. A majority (22/27 or 81%) of patients improved their exercise tolerance after EECP treatment, and a similar percentage (21/27 or 78%) of patients improved their radionuclide stress perfusion images. Post-ECCP maximal exercise heart rate and blood pressure, while demonstrating a linear relation with exercise duration, did not increase significantly despite the increased exercise duration. This suggests that the increase in exercise duration after treatment with EECP is due to both improved myocardial perfusion and altered exercise hemodynamics. EECP therapy thus appears to exert a 'training' effect, decreasing peripheral vascular resistance and the heart rate response to exercise. Coronary disease patients may improve their exercise tolerance after EECP because of both improved myocardial perfusion and a decrease in cardiac work load.

Introduction

Enhanced external counterpulsation (EECP) is a non-invasive treatment for coronary artery disease. EECP uses sequential diastolic inflation of lower extremity pneumatic cuffs to augment aortic diastolic pressure, increase venous return to the heart and decrease left ventricular afterload [1, 2]. Augmenting aortic diastolic pressure increases the coronary artery perfusion pressure and transmyocardial pressure gradient possibly enhancing coronary collateral development. Previous reports have demonstrated both short-term and sustained improvement in radionuclide exercise-induced reversible defects following EECP therapy in a majority of patients [3, 4]. In accord with this finding, patients report subjectively fewer and less severe anginal episodes and an improved exercise tolerance after treatment.

The present study was performed to quantitate the improvement in exercise tolerance in a group of chronic stable angina patients treated with EECP and to assess the effect of EECP treatment on exercise hemodynamics.

Supported by grants from the William E. Pritchard Charitable Trust, Vasogenics and Vasomedical.

KARGER
E-Mail karger@karger.ch
Fax + 41 61 306 12 34
http://www.karger.ch

0008–6312/96/0874–0271$10.00/0

William E. Lawson, MD
State University of New York
Health Sciences Center T-17-020
Stony Brook, NY 11794-8171 (USA)

Received:
October 11, 1995
Accepted:
October 18, 1995

Table 1. Exercise parameters of EECP-treated patients (n = 27; means ± SEM)

	Before EECP	After EECP	Significance
Exercise duration, min	7.17±0.53	8.84±0.50	$p<0.0005$
Maximal HR, beats/min	121.9±5.2	126.3±4.7	NS
Maximal BP, mm Hg	172.3±4.8	164.6±5.2	NS
Maximal DP, beats/min × mm Hg	21,307±1,280	21,166±1,304	NS

HR = Heart rate; BP = blood pressure; DP = double product.

Table 2. Exercise parameters of patients demonstrating improved perfusion imaging after EECP (n = 21; means ± SEM)

	Before EECP	After ECCP	Significance
Exercise duration, min	7.22±0.63	9.12±0.60	$p<0.0005$
Maximal HR, beats/min	117.8±6.0	127.9±5.7	$p<0.05$
Maximal BP, mm Hg	172.0±5.9	170.5±5.6	NS
Maximal DP, beats/min × mm Hg	20,653±1,550	22,240±1,554	NS

For abbreviations, see table 1.

Methods

Patients

Enrolled patients had chronic stable angina (despite prior surgery or medical treatment), angiographic coronary disease (>70% stenosis in a major vessel) and exercise-induced reversible radionuclide perfusion defect(s). Patients were excluded if they had: unstable angina, myocardial infarction within the preceding 3 months, clinical congestive failure, significant valvular heart disease, significant arrhythmia or permanent pacemaker, nonischemic cardiomyopathy, severe peripheral vascular disease, active or recurrent thrombophlebitis, uncontrolled hypertension (>180/110 mm Hg) or bleeding diathesis.

Protocol

A maximal radionuclide stress test was performed prior to entry into the study. The patients received 35 h of treatment with EECP (1–2 h/daily) followed by radionuclide stress testing to the same cardiac work load as baseline and a maximal stress test. No risk factor modifications were introduced during treatment. The patients were maintained on their prestudy cardiac medications.

Radionuclide images were independently evaluated by two observers blinded to patient identities. Images were classified as being unimproved or improved (partial or complete resolution of reversible perfusion defects). The maximal pre- and post-EECP stress tests were analyzed for changes in duration, maximal heart rate and blood pressure response.

Pre- and post-maximal-stress results were compared using the paired two-tailed Student's t test. The subgroups of patients showing improved and unimproved radionuclide stress tests were analyzed separately using the paired two-tailed Student's t test and compared using the unpaired Student's t test. The data were also analyzed using linear regression to evaluate the correlation (Pearson's product-moment correlation coefficient and Spearman's rank correlation coefficient) of change in exercise tolerance with changes in heart rate, blood pressure and double product during maximal exercise in all patients.

Results

There were 26 men and 1 woman treated with a mean age of 60 years (range of 46–73 years). Radionuclide stress perfusion imaging improved in 21 patients and remained unimproved in 6 patients after treatment with EECP.

Exercise duration on the Bruce protocol maximal stress test improved significantly from 7.17 ± 0.53 min before EECP to 8.84 ± 0.49 min after EECP ($p<0.0001$). An improved exercise tolerance was seen after treatment in 22 out of the 27 patients (81%). Pre- and post-EECP heart rate, blood pressure and double product (table 1) did not change significantly.

Examining the subgroup of patients with improved post-EECP perfusion imaging demonstrated significant increases in maximal exercise duration from 7.22 ± 0.63 to 9.12 ± 0.60 min ($p < 0.0005$) and in peak heart rate from 117.8 ± 6.0 to 127.9 ± 5.7 beats/min ($p < 0.05$; table 2) between pre- and post-EECP testing. Peak blood pressure and double product did not significantly differ between pre- and post-EECP testing.

In the subgroup of patients with unimproved perfusion imaging there were no significant differences before or

Table 3. Exercise parameters of patients demonstrating unimproved perfusion imaging after EECP (n = 6; means ± SEM)

	Before EECP	After EECP	Significance
Exercise duration, min	7.01 ± 0.97	7.89 ± 0.61	NS
Maximal HR, beats/min	136.3 ± 9.2	120.7 ± 6.9	NS
Maximal BP, mm Hg	173.3 ± 8.1	140.0 ± 8.9	$p = 0.06$
Maximal DP, beats/min × mm Hg	23,597 ± 1,830	17,404 ± 1,529	$p < 0.05$

For abbreviations, see table 1.

Table 4. EECP treatment effect on hemodynamics in improved (n = 21) and unimproved (n = 6) treatment groups

Change in	Improved group (n = 21)	Unimproved group (n = 6)	Significance
Exercise duration, min	1.90 ± 0.41	0.88 ± 0.74	NS
Heart rate, beats/min	10.1 ± 3.8	−15.7 ± 8.8	$p < 0.01$
Blood pressure, mm Hg	−1.5 ± 5.9	−29.3 ± 12.2	$p < 0.05$
Double product, beats/min × mm Hg	1,588 ± 1,046	−6,193 ± 2,352	$p < 0.005$

after EECP treatment in exercise duration, maximal heart rate or maximal systolic blood pressure (table 3). There was, however, a significant decrease in the post-EECP maximal double product.

Comparison of the improved and unimproved subgroups before and after EECP showed significant differences in the change in maximal heart rate, the change in peak blood pressure and the change in maximal double product. There was no significant difference in the change in exercise duration between the two groups (table 4).

Simple linear regression plots of changes in duration against changes in maximal heart rate, blood pressure and double product (fig. 1–3) demonstrate linear relations with changes in heart rate and blood pressure. The curves are, however, shifted upwards, with an increase in exercise duration over baseline noted for the same heart rate, double product or blood pressure. Correlation coefficients for all patients are presented in table 5.

Table 5. Correlation of change in exercise duration with maximal stress hemodynamic parameters (n = 27)

Change in	Pearson's correlation (r)	Spearman's correlation (r)
Heart rate	0.601	0.620
Blood pressure	0.204	0.204
Double product	0.509	0.446

Discussion

Increasing exercise duration in most circumstances is associated with parallel increases in heart rate and blood pressure. In our group of EECP patients there was a significant increase in overall exercise tolerance and in maximal heart rate in the improved perfusion group. The mean maximal blood pressure, however, actually decreased, though not significantly so, overall and in both subgroups.

If the relation of exercise hemodynamics to exercise duration were unchanged after EECP treatment, an increased exercise tolerance would be associated with an increase in heart rate, blood pressure and double product, and a decreased exercise tolerance would be associated with a decrease in heart rate, blood pressure and double product. Figures 1–3 should show points distributed in the upper right and lower left quadrants with the linear regression line intersecting 0.0 if this relation were true. However, despite decreases in peak exercise hemodynamic measures in many patients, exercise tolerance consistently improved. Regression analysis demonstrates (fig. 1–3) an upward shift in the y intercept, an increased exercise duration, for any given change in hemodynamic mea-

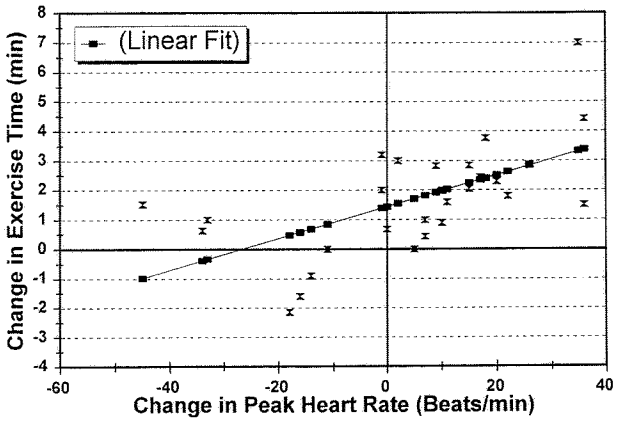

Fig. 1. Change in exercise time versus peak heart rate. The change in maximal exercise duration (in minutes) after EECP treatment is plotted versus the change in maximal heart rate response (in beats per minute). A linear fit is calculated.

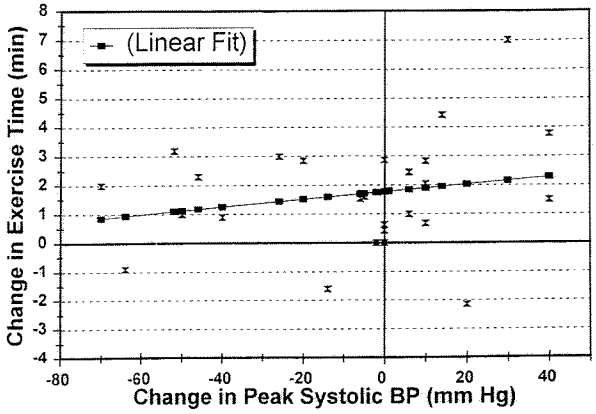

Fig. 2. Change in exercise time versus peak blood pressure. The change in maximal exercise duration (in minutes) after EECP treatment is plotted versus the change in maximal blood pressure response (in millimeters Hg). A linear fit is calculated.

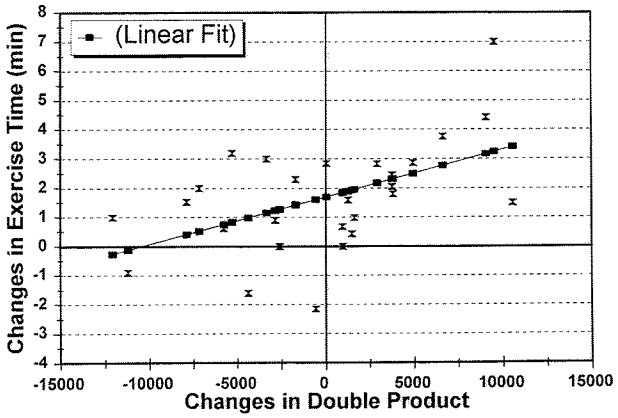

Fig. 3. Change in exercise time versus double product. The change in maximal exercise duration (in minutes) after EECP treatment is plotted versus the change in maximal double product response (maximal heart rate × blood pressure; millimeters Hg × beats per minute). A linear fit is calculated.

sure. Changes in maximal heart rate and maximal double product demonstrate linear correlations with changes in exercise duration.

These findings may imply that EECP has affected systemic vascular resistance, blunting the normal increases in blood pressure and heart rate with exercise. Since the onset of myocardial ischemia is related to myocardial oxygen requirements, reflected clinically as the double product (heart rate × systolic blood pressure), a blunting of the blood pressure and heart rate response to exercise would be expected to delay the onset of myocardial ischemia and improve exercise tolerance.

While significant increases in the heart rate with maximal exercise were demonstrable in those patients showing improved myocardial perfusion and correlated with the increase in exercise duration, the increases in exercise duration were associated with lower than expected heart rates and without significant increases in the blood pressure.

EECP treatment improved myocardial stress radionuclide perfusion in a majority of patients (78%; 21/27 patients). Improvement in myocardial perfusion would be expected to normalize the left ventricular ejection fraction, stroke volume and cardiac output response to exercise in patients with significant coronary artery disease. This would be expected to improve exercise tolerance and generate parallel increases in exertional heart rate and blood pressure. An attenuated heart rate response to exercise may be due to drug effect, chronotropic insufficiency, increases in stroke volume and conditioning. Similarly, an absence of blood pressure response to increasing exercise may be due to drug effect, left ventricular dysfunction or decreased peripheral vascular resistance. However, cardiac drug therapy was held constant and myocardial

perfusion improved, making a drug effect, left ventricular dysfunction or chronotropic insufficiency unlikely. A decrease in peripheral resistance with resultant increased stroke volume, by contrast, cannot be excluded.

The present study suggests that the increase in exercise duration after treatment with EECP is a result of both an improvement in myocardial perfusion (demonstrated by improved stress radionuclide perfusion) and a decrease in peripheral vascular resistance (similar to the training effect of exercise). The two proposed mechanisms are complementary and may explain the symptomatic improvement in patients with unchanged stress perfusion imaging.

References

1 Soroff HS, Hui JCK, Giron F: Current status of external counterpulsation. Crit Care Clin 1986; 2:277–295.

2 Zheng ZS, Yu LQ, Cai SR, Kambic H, Li TM, Ma H, Chen PZ, Huang BJ, Nose Y: New sequential external counterpulsation for the treatment of acute myocardial infarction. Artif Organ 1984;8:470–477.

3 Lawson WE, Hui JCK, Soroff HS, Zheng ZS, Kayden DS, Sasvary D, Atkins H, Cohn PF: Efficacy of enhanced external counterpulsation in the treatment of angina pectoris. Am J Cardiol 1992;70:859–862.

4 Lawson WE, Hui JCK, Zheng ZS, Oster Z, Katz J, Diggs P, Burger L, Cohn C, Soroff HS, Cohn PF: Three-year sustained benefit from enhanced external counterpulsation in chronic angina pectoris. Am J Cardiol 1995;75:840–841.