

Effect of Enhanced External Counterpulsation on Resting Oxygen Uptake in Patients Having Previous Coronary Revascularization and in Healthy Volunteers

Anthony B. Ochoa, MD^{a,*}, Adam deJong, MA^b, Dianna Grayson, RRT, CET^b,
Barry Franklin, PhD^b, and Peter McCullough, MD^b

This study analyzed the acute effects of enhanced external counterpulsation (EECP) on oxygen uptake (VO_2) at rest in adults with symptomatic coronary artery disease (CAD) compared with healthy volunteers. EECP therapy increases exercise tolerance in patients with refractory angina pectoris. This may be attributed, at least in part, to a training effect, but measurement of VO_2 during an EECP treatment session has not been previously reported. We measured VO_2 continuously in 20 adults during a single treatment session of EECP, including 10 subjects with previous coronary revascularization who were referred for EECP therapy for refractory angina, and 10 healthy, sedentary volunteers. VO_2 was measured for 10 minutes before EECP, during a 30-minute EECP treatment session, and for 10 minutes after cessation of EECP treatment. Patients with CAD were older (65.9 ± 12 vs 38.5 ± 7 years, $p = 0.002$) and had a higher body mass index (32.0 ± 10.0 vs 25.5 ± 3.0 kg/m^2 , $p = 0.027$) and percent body fat ($37 \pm 7\%$ vs $21 \pm 9\%$, $p = 0.006$). VO_2 at rest, although slightly lower in the CAD group, was not significantly different (2.75 ± 0.54 vs 3.19 ± 0.51 ml/kg/min , $p = 0.09$). The 2 groups demonstrated a small, sustained increase in VO_2 during EECP treatment (CAD $+0.66 \pm 0.56$ ml/kg/min , $p < 0.005$; healthy $+0.72 \pm 0.40$ ml/kg/min , $p < 0.001$; CAD vs healthy, $p = 0.13$), which returned to baseline levels during recovery. In conclusion, VO_2 at rest is increased to the same degree during an EECP treatment session in healthy subjects and symptomatic patients with CAD. This effect may contribute to the increased exercise tolerance of patients with refractory angina after receiving EECP therapy. © 2006 Elsevier Inc. All rights reserved. (Am J Cardiol 2006;98:613–615)

Several studies have reported variable changes in the rate–pressure product during exercise treadmill testing after completing a typical course of enhanced external counterpulsation (EECP) therapy.^{1–4} Inconsistent findings concerning this clinical end point are not surprising and probably reflect differences in patients (motivation, use of medications to modulate heart rate and blood pressure, presence of concomitant pulmonary disease) and in study design (maximal stress testing vs a predetermined workload target before and after EECP therapy). Although peak or maximal oxygen uptake ($\text{VO}_{2\text{max}}$) is considered the most accurate measurement of a patient's cardiorespiratory fitness and conditioning response to aerobic exercise training,⁵ this variable has not been studied in clinical trials of EECP for patients with chronic refractory angina. For EECP to exert a direct training effect and thus contribute to any potential increase in

$\text{VO}_{2\text{max}}$, somatic VO_2 at rest would be expected to increase acutely during EECP treatment sessions. Therefore, we tested the hypothesis that EECP simulates low-intensity exercise by continuously measuring VO_2 during a single EECP therapy session performed in patients with previous coronary revascularization and refractory angina who were referred for EECP therapy compared with healthy subjects.

Methods

Twenty men and women participated in this study. The study protocol was approved by the human investigation committee of William Beaumont Hospital (Royal Oak, Michigan), and all subjects gave written, informed consent before participating. Patients with angiographically proven coronary artery disease (CAD) who were referred for EECP therapy for refractory angina pectoris were invited to participate, and 10 were enrolled (CAD group, $n = 10$). This group comprised patients at various stages of completion of the typical 7-week course of EECP therapy. Healthy, sedentary patients (exercise ≤ 2 sessions/week) were recruited to assess the effect of muscle conditioning provided by EECP in a cohort representing an “average” healthy adult in the United States population as a reference for comparison. Healthy subjects were screened for the following exclusion criteria: known CAD or any traditional risk factors for CAD

The ^aWright-Patterson Medical Center, Wright-Patterson AFB, Ohio; and the ^bWilliam Beaumont Hospital, Royal Oak, Michigan. Manuscript received January 4, 2006; revised manuscript received and accepted March 21, 2006.

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*Corresponding author: Tel: 937-257-1817; fax: 937-257-1819.

E-mail address: anthony.ochoa@wpafb.af.mil (A. Ochoa).

Table 1
Demographic and baseline characteristics

Variable	Healthy Sedentary (n = 10)	CAD (n = 10)*	p Value
Age (yrs)	38.5 ± 7	65.9 ± 12	0.002
Women	3	3	1.00
Height (cm)	173 ± 10	173 ± 8	0.71
Weight (kg)	76 ± 15	87 ± 8	0.12
Body surface area (m ²)	1.9 ± 0.4	2.1 ± 0.3	0.002
Body mass index (kg/m ²)	25.5 ± 3.0	32.0 ± 10.0	0.027
Body fat (%)	21 ± 9	37 ± 7	0.006
Previous coronary artery bypass grafting	0	8	<0.001
β-Blocker use	0	8	<0.001
VO ₂ at rest (mL/kg/min)	3.19 ± 0.51	2.75 ± 0.54	0.09

Values are expressed as mean ± SD.

* All patients had previous coronary revascularization; 8 had undergone coronary artery bypass grafting, with or without previous percutaneous transluminal coronary angioplasty, whereas the remaining 2 had undergone multiple angioplasty procedures.

(hypertension, tobacco use, family history of early-onset CAD, diabetes mellitus, hyperlipidemia), known long-term illness, and exercise of any duration >2 times/week. Ten subjects were enrolled in the healthy control group.

VO₂ was measured (Medgraphics CPX/D, Medical Graphics Corp., Minneapolis, Minnesota) continuously for 10 minutes before EECP (VO₂ at rest), during a 30-minute EECP treatment session (EECP-VO₂), and for 10 minutes after cessation of EECP treatment (recovery VO₂). The metabolic measurement system includes a computer assembly for breath-by-breath and online, 60-second calculations of VO₂, minute ventilation, carbon dioxide output, and respiratory exchange ratio. Before each test, the pneumotachometer was referenced according to manufacturer's specifications with a 3-L syringe, and the gas analyzers were calibrated with certified air mixtures. A standard mouthpiece with saliva trap was employed.

EECP treatment was performed with the TS3 EECP treatment system (Vasomedical, Inc., Westbury, New York). After preliminary familiarization to allow habituation of the open-circuit spirometry and heartbeat-synchronized EECP treatment, study participants were asked to refrain from talking, changing position, or moving on the treatment table during testing. EECP treatment was resumed for the CAD group for an additional 30 minutes once VO₂ measurements were made to complete a full 60-minute daily EECP treatment session as prescribed. EECP treatment was performed with maximal external compression (280 mm Hg) delivered through 3 sets of cuffs applied to the buttocks, thighs, and legs, with optimal timing adjustments of cuff inflation and deflation, as per the manufacturer's recommendations to achieve maximal diastolic augmentation for all study participants. Noninvasive, unassisted blood pressures for all subjects were recorded at 5-minute intervals during the resting and EECP recovery phases and once midway (15 minutes) during the active EECP phase, with the TS3 device paused briefly. Heart rate was monitored

continuously by finger plethysmography, and values were recorded every 5 minutes during all phases of testing.

All statistical analyses were performed with SAS 8 (SAS Institute, Cary, North Carolina). Group data are expressed as mean ± SD for continuous variables. Continuous variables were assessed with Wilcoxon's rank-sum test. Categorical variables were examined with Fischer's exact 2-sided test. Statistical significance was defined as a p value <0.05.

Results

Demographics and baseline characteristics for the 2 groups are presented in Table 1. Mean VO₂ at rest was lower in the CAD group, which may reflect the use of β-blocking agents, but this trend did not reach statistical significance. Changes in physiologic parameters for the 2 groups during active EECP and EECP recovery phases are presented in Table 2. Participants with CAD and healthy subjects demonstrated a small, but significant increase in VO₂ during active EECP treatment. The relative increase in VO₂ was identical in the 2 groups, remained high throughout active treatment, and returned to levels at rest after cessation of EECP (Figure 1). EECP was well tolerated by all subjects, and no adverse events occurred in either group.

Discussion

We have demonstrated for the first time that EECP acutely increases VO₂ at rest in a small, but sustained fashion during a single therapy session in patients with refractory angina and in healthy sedentary adults. The magnitude this increase equates to is a very low level of exertion and would not be expected to induce a significant training effect despite the long duration of EECP therapy (35 60-minute sessions completed over 7 to 8 weeks). However, recent studies have suggested that the threshold or minimal effective intensity for increasing cardio-respiratory fitness in unfit and fit patients with and without CAD is lower than previously believed, approximating 30% to 45% of the VO₂ reserve.^{6,7} Thus, EECP therapy may serve as a sufficient aerobic stimulus for training among unfit patients with refractory angina.

The simulation of a very low level of exercise by EECP, in conjunction with its other beneficial cardiac and vascular effects, may promote increased exercise tolerance as reported by several clinical trials of EECP in patients with refractory angina without necessarily resulting in increased VO_{2max}.¹⁻⁴ At our institution, we have had many anecdotal reports by patients of fatigue induced by EECP therapy similar to that induced by structured exercise. The relative contribution this "passive exercise" effect may have to the clinical benefits from EECP in patients with refractory angina is difficult to assess because the mechanism of action of EECP is likely multifactorial.⁸ Cardiac output, left ventricular diastolic filling time, and coronary flow reserve have been demonstrated to increase with EECP and, because of the results of our study, probably contribute more toward increasing functional capacity than the peripheral training effect.^{3,4,9}

Table 2
Changes in physiologic parameters during external counterpulsation

Physiologic Parameter	Healthy Sedentary (n = 10)	CAD (n = 10)	p Value
Systolic blood pressure at rest (mm Hg)	112 ± 14	126 ± 16	0.044
Systolic blood pressure at 30 minutes (mm Hg)	110 ± 13	122 ± 20	0.12
Δ systolic blood pressure (mm Hg)	-1.6 ± 9 (p = 0.59)	-3.2 ± 11 (p = 0.39)	0.65
Diastolic blood pressure at rest (mm Hg)	70 ± 10	72 ± 9	0.58
Diastolic blood pressure at 30 minutes (mm Hg)	78 ± 9	77 ± 11	1.00
Δ Diastolic blood pressure (mm Hg)	8.0 ± 5.2 (p = 0.0009)*	5.2 ± 5.3 (p = 0.013)*	0.30
Heart rate at rest (beats/min)	68 ± 12	61 ± 9	0.32
Heart rate at 15 min (beats/min)	75 ± 13	62 ± 11	0.032*
Heart rate at 30 min (beats/min)	73 ± 11	64 ± 13	0.13
Heart rate at recovery (beats/min)	68 ± 12	64 ± 15	0.39
Δ Heart rate (30 min at rest) (beats/min)	7.2 ± 9.5 (p = 0.04)*	2.9 ± 7.6 (p = 0.26)	
VO ₂ at rest (ml/kg/min)	3.19 ± 0.51	2.75 ± 0.54	0.090
EECP VO ₂ (ml/kg/min)	3.91 ± 0.58	3.41 ± 0.95	0.068
Recovery VO ₂ (ml/kg/min)	3.13 ± 0.59	2.64 ± 0.62	0.10
Δ VO ₂ (ml/kg/min)	+0.72 ± 0.40 (p = 0.0003)*	+0.66 ± 0.56 (p = 0.005)*	0.13

Values are expressed as mean ± SD.

* Signifies a statistically significant difference.

Δ = change.

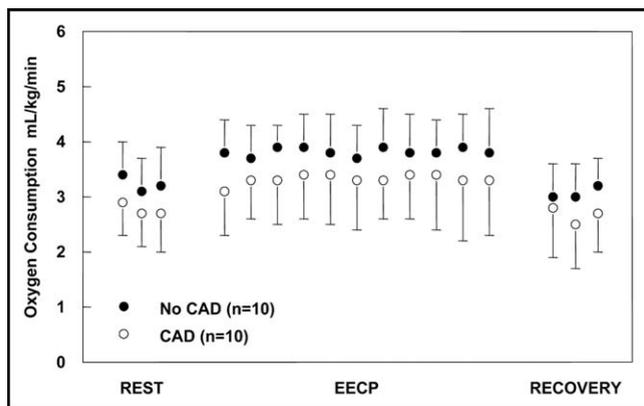


Figure 1. Mean changes ± SD in VO₂ at rest during an EECP therapy session in patients with previous coronary revascularization and in healthy control subjects.

The EECP-induced augmentation in metabolic rate at rest occurred to the same degree in healthy, albeit sedentary, volunteers as in those patients with refractory angina, irrespective of their type/frequency of previous coronary revascularization. If this finding is eventually translated into increased functional capacity for “noncardiac” patients, EECP could be applied to other disease states and disabling conditions. Many patients who are referred for EECP therapy cannot participate in traditional exercise-based cardiac rehabilitation due to their inability to perform even minimal activity without provoking anginal symptoms. In our experience, most of these patients can be referred to a phase 2 cardiac rehabilitation program after completion of EECP therapy and/or to a home-based exercise regimen. Despite the elusiveness of its exact mechanism of action for long-term benefit in most patients who receive EECP therapy, it has become increasingly used in the treatment of patients with ischemic heart disease and may soon expand beyond this indication.

Some limitations should be considered when interpreting the results of this preliminary investigation. The study was primarily limited by its small sample. In addition, we measured VO₂ before, during, and after a single EECP treatment session for each participant. Thus, the effect of repeated EECP on VO₂ over time remains unknown.

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