2013


Enhanced external counterpulsation (EECP) increases coronary artery perfusion and improves endothelium-dependent vasodilation in peripheral muscular conduit arteries. It is unknown whether vasodilatory capacity is improved in the peripheral resistance vasculature. Here we provide novel evidence from the first randomized, sham-controlled study that EECP increases peak limb blood flow and improves endothelium-dependent vasodilation in both calf and forearm resistance arteries in patients with coronary artery disease (CAD).


Background: Refractory angina pectoris (AP) is a persistent, painful condition characterized by angina caused by coronary insufficiency in the presence of coronary artery disease. It has been emphasized that there are possible underlying neuropsychophysiological mechanisms for refractory AP but chronic ischemia is still considered to be the main problem. These patients suffer from severe AP and cannot be controlled by a combination of pharmacological therapies, angioplasty or coronary bypass surgery. AP has a negative impact on quality of life and daily life. Enhanced external counterpulsation (EECP) is a therapeutic option for these patients. Aims: The aim of this study was to evaluate EECP after six months regarding physical capacity and health-related quality of life (HRQoL) in patients with refractory AP. Methods: This was a study with single case research experimental design involving 34 patients treated with EECP. Six minute walk test (6MWT), functional class with Canadian Cardiological Society (CCS) classification and self-reported HRQoL questionnaires as Short Form 36 (SF-36) were collected at baseline and after treatment. CCS class and SF-36 were repeated at six months follow-up. Results: Patients enhanced walk distance on average by 29 m after EECP (p<0.01). CCS class also improved (p<0.001) and persisted at six months follow-up (p<0.001). HRQoL improved significantly and the effects were maintained at follow-up after the treatment. Conclusion: Patients with refractory AP receive beneficial effects from EECP both in physical capacity and HRQoL. As other treatment options for this patient group are scarce, EECP should be offered to improve physical health and HRQoL in these patients.


Background: Despite treatments, some patients with chronic refractory angina continue to experience disabling symptom. This study investigated the safety and effectiveness of enhanced external counterpulsation (EECP) in treating patients who had had a previous transmyocardial laser revascularization (TMR). Methods: Patients in the International EECP Patient Registry I and II were divided into those who had a prior TMR, those who had a prior percutaneous or surgical revascularization (PCI/CABG) and those who had medical therapy alone (Medical). Their baseline characteristics, treatment outcome and clinical events were compared. Results: Of the 4,306 patients, 91 had a prior TMR, 3,790 had a prior PCI/CABG and 425 were treated with medicat therapy with no previous invasive revascularization procedures. Patients in the TMR were younger compared to PCI/CABG and Medical patients (62 ± 12 versus 67 ± 11 and 68 ± 13 years respectively, p<0.001), and more of them had multi-
vessel coronary disease (92% versus 84% and 62%, respectively, p<0.001), with longer duration of disease (13 ± 9 versus 12 ± 8 and 7 ± 9 years respectively, p<0.001). Most patients were unsuitable to have a further conventional revascularization (TMR 91% versus PCI/CABG 89% and Medical 82%, p<0.001). At baseline, more TMR patients had CCS III/IV angina (98% versus PCI/CABG 92% and Medical 87%, p<0.01) with more frequent angina and nitroglycerine (GTN) use than the others. Compared to PCI/CABG and Medical patients, fewer TMR patients completed their EECP course (75% versus 83% and 85% respectively, p<0.05), and had higher rate of unstable angina (11% versus 4% and 2% respectively, p<0.001) and myocardial infarction (5% versus 1% and 1% respectively, p<0.01) during the 7-week of EECP treatment period. Compared to PCI/CABG and Medical patients, fewer TMR had improvement in CCS (66% versus 76% and 79% respectively, p<0.05) and discontinuation of GTN (33% versus 49% and 54% respectively, p<0.001) immediately post-EECP. Using multivariate logistic regression analysis, 35 hours or more EECP treatment was associated with an improvement in CCS class post-EECP whilst prior TMR, CABG and milder pre-EECP angina were associated with a lack of improvement. After 1 year, 3 TMR, 201 PCI/CABG and 28 Medical patients died. Of those who survived, sustained improvement in CCS was seen in 68% TMR, 76% PCI/CABG and 87% Medical patients, p<0.001. TMR patients had higher repeat EECP rate and trended to have higher major adverse cardiovascular event rate when compared to PCI/CABG and Medical patients (25% versus 17% and 17%, p<0.01 and 14% versus 8% and 5%, p=0.14 respectively). Conclusion: Although patients who have a prior TMR suffer from more advanced coronary artery disease and consequently higher adverse event rates, a large proportion of them will benefit from EECP.


**Background:** To investigate the therapeutic value of enhanced external counterpulsation (EECP) on recovery of cerebral blood flow following cardiac arrest (CA) and successful resumption of spontaneous circulation (ROSC) by cardiopulmonary resuscitation. Methods: CA models were conducted using beagle dogs induced by alternating current. After successful ROSC by cardiopulmonary resuscitation, 16 dogs were randomly divided into the EECP and control group (n = 8 per group). Dogs underwent dynamic contrast-enhanced and diffusion-weighted magnetic resonance imaging at baseline prior to CA and during the 3 days following ROSC. Mean blood pressure, right common carotid artery blood flow, intracranial microcirculation and blood lactate levels were measured. Neurological outcome was assessed by the neurologic deficit score. Hematoxylin-eosin staining and transmission electron microscopy were performed for morphology and microconstruction of the cerebral cortex. Results: The EECP group exhibited a significant elevation in right common carotid artery blood flow, intracranial microcirculation and a substantial decrease in blood lactate levels relative to the control group. Relative cerebral blood flow and volume were higher in the EECP group during the 3 days. Apparent diffusion coefficients were significantly higher in the EECP group on the first and third days. After ROSC, the neurologic deficit score was significantly higher in the control group compared to those in the EECP group during the three days of experiment. The cell swelling of neurons and increase of mitochondrial mass were more pronounced in the control group. Conclusion: EECP is beneficial for recovery of cerebral blood flow and attenuation of ischemic cerebral edema following CA and successful ROSC.


**Background:** Enhanced external counterpulsation (EECP) enhances coronary perfusion and reduces left ventricular afterload. However, the role of EECP on renal function in cardiac patients is unknown. Our aim was to assess renal function determined by serum cystatin C in cardiac patients before and after EECP treatment. Methods: A prospective observational longitudinal study was conducted in order to evaluate renal function using serum cystatin C (Cys C) and estimated glomerular filtration rate (GFR) after 35
sessions of EECP treatment in 30 patients with chronic stable angina and/or heart failure. The median (IQR) time for follow-up period after starting EECP treatment was 16 (10–24) months. Results: Cys C significantly declined from 1.00 (0.78–1.31) to 0.94 (0.77–1.27) mg/L (p < 0.001) and estimated GFR increased from 70.47 (43.88–89.41) to 76.27 (49.02–91.46) ml/min/1.73 m² (p = 0.006) after EECP treatment. Subgroup analysis showed that patients with baseline GFR <60 ml/min/1.73 m² or NT-proBNP >125 pg/mL had a significant decrease in Cys C when compared to other groups (p < 0.01). Conclusions: The study demonstrated that EECP could improve long-term renal function in cardiac patients especially in cases with declined renal function or with high NT-proBNP.


Background: Chronic heart failure (CHF) is a slowly progressive disease with high morbidity and mortality; therefore, the management using pharmacological treatments frequently fails to improve outcome. Enhanced external counterpulsation (EECP), a non-invasive treatment, may serve as alternative treatment for heart failure. This study was aimed to evaluate the influence of EECP on myeloperoxidase (MPO) as inflammatory marker as well as cardiac events outcome. Methods: This was an open randomized controlled clinical trial on 66 CHF patients visiting several cardiovascular clinics in Manado between January-December 2012. The subjects were randomly divided into two groups, i.e. the group who receive EECP therapy and those who did not receive EECP therapy with 33 patients in each group. Myeloperoxidase (MPO) as inflammatory marker was examined at baseline and after 6 months of observation. Cardiovascular events were observed as well after 6 months of observation. Unpaired t-test was use to analyze the difference of MPO between the two groups, and chi-square followed by calculation of relative risk were used for estimation of cardiovascular event outcomes. Results: MPO measurement at baseline and after 6 months in EECP group were 643.16 ± 239.40 pM and 422.31 ± 156.26 pM, respectively (p < 0.001). Whereas in non EECP group, the MPO values were 584.69 ± 281.40 pM and 517.64 ± 189.68 pM, respectively (p = 0.792). MPO reduction was observed in all patients of EECP group and in 13 patients (48%) of non-EECP group (p < 0.001). Cardiovascular events were observed in 7 (21.21%) and 15 (45.45%) of patients in EECP and non-EECP groups, respectively (p = 0.037). Conclusion: EECP therapy significantly decreased the level of MPO as inflammatory marker and this decrease was correlated with the reduction of cardiovascular events in CHF patients.

- **Ashkan Eftekhari, Ole May. Effect of enhanced external counterpulsation depends on arterial compliance, Acta Cardiol 2013;68(1):47-50.**

Enhanced external counterpulsation (EECP) is a non-invasive therapy offered to patients with refractory angina pectoris. Previous studies have demonstrated that its clinical effect depends on the diastolic/systolic augmentation ratio (D/S ratio). We hypothesized that the D/S ratio is associated with arterial stiffness measured as pulse wave velocity (PWV) and brachial pulse pressure (PP). Twenty patients with known refractory angina (17 men, 3 women; mean age 64 years) were included and underwent one hour of EECP treatment (Vasomedical Inc., Westbury, NY, USA). Three sets of cuffs were applied around the lower extremities. Gated by electrocardiography (ECG), air was inflated in diastole at a pressure of 260 mmHg and deflated at the start of systole. The D/S ratio was monitored with finger plethysmography. Carotid-femoral pulse wave velocity (PWV) was measured with mechanotransducers (Compilior SP, Artech Medical, France). PWV and brachial BP were measured at baseline before EECP. The mean (SD) BP was 140 (23.5)/77 (9.9) mmHg, PP 62.8 (18.3) mmHg and PWV 10.8 (4.4) m/s. EECP treatment increased the D/S ratio during a one-hour session compared with baseline (1.30 (0.11) vs. 0.56 (0.04) P < 0.001), and the D/S ratio at 45 min. was significantly correlated with PWV (r = 0.49, P < 0.05) and PP (r = 0.58, P < 0.05). We demonstrated that the diastolic augmentation (D/S ratio) during EECP treatment depends on arterial stiffness. The results suggest that arterial compliance has a crucial influence on the effect of EECP and that large-artery stiffness may reduce the effect of EECP.
• **Debra L Braverman, Len Braitman, Vincent M Fifeuredo. The Safety and Efficacy of Enhanced External Counterpulsation as a Treatment for Angina in Patients with Aortic Stenosis. Clin Cardiol 2013;36(2):82-87.**

**Background:** Comorbid aortic stenosis (AS) has been considered a precaution when applying enhanced external counterpulsation (EECP) to individuals with angina due to concerns about treatment-related hemodynamic changes. **Hypothesis:** The aim of this study was to determine whether EECP safety reduces symptoms of myocardial ischemia improves hemodynamics in individuals with AS. **Methods:** Forty-three patients with AS (average age, 73 years; 86% male) and 43 comparison patients without AS were chosen from a database of 1327 EECP patients. Canadian Cardiovascular Society (CCS) Functional Angina Classification, diastolic augmentation ratio, and blood pressure were measured at baseline and on completion of the course of EECP. Results: Thirty-five of the 43 patients with AS (81%, 95% CI: 66.6% to 91.6%) and 38 of the 43 without AS (88%, 95% CL: 74.9% to 96.1%) improved in angina class (p<0.0001). There was no statistical difference between the percentages in patients with and without AS (p=0.54). CCS angina class outcome was not associated with AS severity (p=0.55). The percentage of patients with diastolic augmentation ratio ≥ 1.0 was 16.3% in both groups at baseline and improved to 39.5% in AS patients and 37.2% in non-AS patients after EECP (both p=0.002). The average decrease in systolic pressure in subjects with AS (-15 mm Hg, 95% CI: 11 to 20, p<0.0001) and without AS (-18 mm Hg, 95% CL: 14 to 22, p<0.0001) were similar (p=0.31). No major adverse cardiac events were reported.


The aim of this study was to evaluate the clinical effect in patients with ocular ischemic diseases treated with enhanced external counterpulsation (EECP) combined with drugs. A total of 65 patients with carotid artery stenosis were included in this study. Group A consisted of 31 patients (43 eyes) treated with EECP and medication, and group B consisted of 34 patients (49 eyes) treated with medication alone. The clinical effect was analyzed by comparing the visual acuity, visual fields and optical hemodynamics between the two groups of patients. Ocular ischemic diseases mainly included ischemic optic neuropathy, central (branch) retinal artery occlusion, ophthalmoplegia externa and ocular ischemic syndrome. Significant improvement of visual acuity, visual fields and optical hemodynamics was observed in the patients of group A, and statistically significant differences were found between groups A and B ($\chi^2$=4.935, 7.124 and 5.478, respectively; p<0.05). In conclusion, ocular ischemic diseases and the symptoms of the disease and the vision of the patient could be effectively improved by EECP. EECP has no incident of complications.

• **Jørgensen MT, May O. Improvement of angina, quality of life, and working capacity after enhanced external counterpulsation. Ugeskr Laeger. 2013 Jan 14;175(3):114-116.**

This case report describes a 43-year-old woman who had had 15 hospital admissions in six years due to chest pain. Repeated coronary angiography showed no significant stenoses, but myocardial scintigraphy revealed reversible ischaemia. In spite of optimal medical treatment, she was in Canadian Cardiovascular Society (CCS) class 3 with a poor quality of life (QoL). After a course of enhanced external counterpulsation the CCS class was reduced to 1, and QoL was significantly improved and remained high for the following three years, resulting in only one hospital admission due to chest pain. The case illustrates that EECP is an efficient therapy for angina pectoris in patients, who are not amenable for invasive procedures.

Objectives: External counterpulsation (ECP) is a non-invasive method being investigated for ischemic stroke. We aimed to explore predictors of good functional outcome for ECP-treated ischemic stroke patients who completed a minimum of 10 sessions. Methods: We analyzed our ECP registry of ischemic stroke patients with cerebral large artery stenosis who underwent ECP therapy at the Prince of Wales Hospital from 2004 to 2010. We included 155 patients who completed at least 10 sessions of ECP and had 3-month follow-up data as well as 52 medical controls. Functional outcomes were dichotomized into good outcome (modified Rankin Scale (mRS) 0–2) and bad outcome (mRS 3–6). We compared the differences in two groups in terms of demographics, medical history and parameters of ECP treatment. Results: At 3 months after stroke, 70.5% of patients who finished the whole course of ECP had a good outcome (only 46.5% in the unfinished group and 38.5% in the medical group). Among all 207 recruited cases, 119 (57.5%) patients had a good outcome at 3 months after stroke. Compared with the bad outcome group, patients in the good outcome group were younger and had a lower baseline National Institutes of Health Stroke Scale (NIHSS) and longer ECP therapy duration. Multivariate logistic regression showed that ECP duration (OR 1.032), baseline NIHSS (OR 0.734) and age (OR 0.961) were independent predictors for a favorable outcome. Conclusions: Duration of ECP therapy is first found to be an important predictor for good outcome of ECP treated ischemic stroke patients, in addition to the well-known prognostic factors such as age and NIHSS.


Objectives: The aim of this study was to investigate whether early enhanced external counter pulsation therapy after cardiopulmonary resuscitation improved neurological outcome in a mongrel dog cardiac arrest model. Subjects: Twenty-four healthy male adult dogs (12-14 kg). Interventions: After minutes of untreated ventricular fibrillation followed by 2 minutes of cardiopulmonary resuscitation, the dogs were randomized to receive 4 hours of enhanced external counter pulsation therapy, to receive 4 hours of hypertension with over 140 mm Hg or to be a control. Measurements: Blood pressure and left ventricular ejection fraction were recorded. Cerebral flow was assessed using magnetic resonance imaging. Arterial blood gases and endothelium-derived vasoactive substances were assessed before cardiac arrest and 4 hours after the return of spontaneous circulation. Neurological outcome was assessed by the neurologic deficit score and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling staining.

Results: Enhanced external counter pulsation significantly improved the left ventricular ejection fraction and increased common carotid artery blood flow and shear stress. Enhanced external counter pulsation increased both relative cerebral blood volume (RCBV, p = 0.043) and relative cerebral blood flow (RCBF, p = 0.012) in animals 4 hours after return of spontaneous circulation. Enhanced external counter pulsation therapy promoted the production of nitric oxide and tissue plasminogen activator and decreased the release of endothelin-1 (p = 0.013) after return of spontaneous circulation. Treatment with norepinephrine in the high mean artery pressure also increased common carotid artery blood flow and shear stress. However, no effects on the left ventricular ejection fraction, the production of nitric oxide and tissue plasminogen activator, or the release of endothelin-1 were found. The neurologic deficit scores of the animals were significantly lower at 24, 48, 72, and 96 hours in the enhanced external counter pulsation group, as well as at 24, 72, and 96 hours compared with animals in the control group after return of spontaneous circulation. Fewer apoptotic neurons were observed in the animals in the enhanced external counter pulsation group compared with the animals in the control and hypertension groups. Conclusions: These data indicated that the treatment of early enhanced external counter pulsation improved neurological outcome by both increasing cerebral blood flow and improving the recovery of microcirculation after return of spontaneous circulation. The treatment of early enhanced external counter pulsation can be a good option for protecting the brain after return of spontaneous circulation.

- Güliz Kozdağ, Pervin İşeri, Gökçen Göçke, Gökhan Ertaş, Fatih Aygün, Ayşe Kutlu, Kathy Hebert, Dilek Ural. Treatment with enhanced external counterpulsation improves cognitive...

Objectives: Chronic heart failure (CHF) has been associated with an increased risk of poorer cognitive performance in older adults. Reversibility of cognitive impairment after medical treatment has been reported, although the restorative effects of enhanced external counterpulsation (EECP) on cognitive performance have not been studied. We investigated the effect of EECP on cognitive functions in CHF patients. Study design: Thirty-six individuals (mean age: 66±8 years) who were diagnosed with CHF and were New York Heart Association (NYHA) Class II-III and Canadian Cardiovascular Society (CCS) Class II-III participated in this study. Neuropsychological assessment was performed in these patients. Results: Patients in the EECP treatment group showed a statistically significant improvement in spontaneous naming (p=0.011) and forward row score of the attention subset among domains of cognition (p=0.020) and interference time of executive function (p=0.012). Conclusion: Enhanced external counterpulsation resulted in improvement in all domains of cognitive functions except verbal and visual memory tests.


Taking into account that discussed above, This is a commentary proposing that a noninvasive evaluation of arterial properties (i.e., arterial stiffness) and functional capabilities (i.e., endothelial function) could have a role in clinical practice in the context of EECP, particularly considering the value/accuracy of the parameters evaluated and that they can be obtained in an easy and quick way with relative low costs for the evaluation of the arterial system before and after EECP would potentially (a) contribute to the understanding of EECP working mechanisms and differences in patient’s capability to respond to the counterpulsation therapy, (b) add information to guide patient’s treatment (i.e., maximize the strategies aimed at modulating arterial load) and (c) aid in patient selection, particularly in those in whom with EECP indication and/or opportunity is discussed.


This is a review paper on collateral circulation stating that external counterpulsation is a therapeutic option to increase shear stress on endothelial cells. It has repeatedly been shown to reduce symptoms in patients with angina pectoris but the mechanism of action has remained unknown for years. The first controlled trial in a group of patients with coronary artery disease undergoing a 30-h program of high-pressure ECP (300 mmHg) and in a group undergoing sham ECP at 80 mmHg inflation pressure has demonstrated a relevant improvement of the collateral function (CFI) between baseline and follow-up at 4 weeks

Background: The purpose of this study was finding relationship between the therapeutic effects of Enhanced External Counterpulsation on treatment resistant angina among the patients, who are unsuitable for invasive interventions. Aims & Objective: To study the therapeutic effects of Enhanced External Counterpulsation (EECP) on clinical symptoms, echocardiographic measurements, perfusion scan parameters and exercise tolerance test in coronary artery disease patients with refractory angina. Material and Methods: In an interventional study 50 patients (34 men and 16 women) under EECP therapy were investigated for one year. This machine is composed of three pairs of cuffs which work by attaching cuffs to lower limbs and it is contracted during diastole from distal to proximal and makes pressure to vessels of lower limbs. Treatment effects of EECP on clinical signs were evaluated on the base of Canadian cardiovascular society classification for angina severity, drugs consumption and SF36 quality of life questionnaire. Para clinical assessments including echocardiography, perfusions scan and exercise tolerance test parameters were also assessed prior to EECP, at the end of the treatment and at 12 months thereafter. Any differences in background measurements were recorded and analyzed. Results: Decrement of angina severity and improvement of life quality before and after one month EECP therapy was significant (p<0.001, p=0.01). The rate of nitrate consumption and other medications causes no significant difference concerning dosage decrease (p>0.05). There was significant difference between ejection fraction of before, one month and one year after treatment only in severe IHD (p=0.016, p=0.038, respectively). Left ventricle end diastolic and end systolic diameters were also significantly decreased after one month (p= 0.031), and this improvement remained up to one year. Difference between ischemia severity in perfusion scan before and one month afterwards was significant as well (p= 0.044). The exercise tolerance test duration after one month also increased (p<0.001) and did not change statistically after one year. Conclusion: This study demonstrated that EECP is a useful method, while effective and safe for patients with severe refractory angina pectoris resistant to drug therapy and aggressive interventions such as PCI or CABG are not suitable.

2012


Background: Enhanced External Counterpulsation (EECP) is a novel; FDA approved; non-invasive; outpatient treatment offered to patients with refractory angina pectoris. It uses sequentially inflated pneumatic cuffs on the lower extremities to enhance coronary diastolic flow. We studied its effect in twenty one patients with refractory angina pectoris. Methods: All patients (n=21) who were referred for Enhanced External Counterpulsation to Shahid Gangalal National Heart Center Enhanced External Counterpulsation Lib who completed a treatment course (one hour per day for 35 days) of EECP and underwent 6-minute walk test before and after treatment were included. Demographic data, coronary artery disease risk factors and baseline angiographic data were collected. Distance covered in six minute walk test before and after the treatment was compared. Results: All the patients who had undergone Enhanced External Counterpulsation had a positive clinical response. Distance covered in six minute walk test improved in all patients after the treatment. Decrease in anginal severity, frequency and the use of sublingual nitrates, with improvement in quality of life was observed after the treatment. During the treatment some patients complained of leg pain, one patient developed blister and one ecchymosis but the treatment was not discontinued. Conclusion: The results from this study suggest that Enhanced External Counterpulsation is an effective, safe and well tolerated treatment option for the patients with refractory angina pectoris.

Elevated markers of systemic inflammation are associated with impaired glucose and type 2 diabetes mellitus. Enhanced External Counterpulsation (EECP) has been shown to decrease circulating concentrations of pro-inflammatory markers in coronary artery disease patients. Here we provide novel evidence that EECP intervention also has a beneficial effect on circulating markers of systemic inflammation coincident with improvement in glycemic control in subjects with abnormal glucose tolerance.

• **Al Kaabi A, Traupe T, Stutz M, Buchs N, Heller M. Cause or Effect of Arteriogenesis: Compositional Alterations of Microparticles from CAD Patients Undergoing External Counterpulsation Therapy. PLoS ONE 7(10): e46822. doi:10.1371/journal.pone.0046822**

Recently, a clinical study on patients with stable coronary artery disease (CAD) showed that external counterpulsation therapy (ECP) at high (300 mmHg) but not at low inflation pressure (80 mmHg) promoted coronary collateral growth, most likely due to shear stress-induced arteriogenesis. The exact molecular mechanisms behind shear stress-induced arteriogenesis are still obscure. This paper characterized plasma levels of circulating microparticles (MPs) from these CAD patients because of their ambivalent nature as a known cardiovascular risk factor and as a promoter of neovascularization in the case of platelet-derived MPs. MPs positive for Annexin V and CD31CD41 were increased statistically significant (p<0.05, vs. baseline) only in patients receiving high inflation pressure ECP as determined by flow cytometry. MPs positive for CD62E, CD146, and CD14 were unaffected. In high, but not in low, inflation pressure treatment, change of CD31CD41 was inversely correlated to the change in collateral flow index (CFI), a measure for collateral growth. MPs from the high inflation pressure group had a more sustained pro-angiogenic effect than the ones from the low inflation pressure group, with the exception of one patient showing also an increased CFI after treatment. A total of 1005 proteins were identified by a label-free proteomics approach from MPs of three patients of each group applying stringent acceptance criteria. Based on semi-quantitative protein abundance measurements, MPs after ECP therapy contained more cellular proteins and increased CD31, corroborating the increase in MPs. Furthermore, MP-associated factors of the innate immune system were decreased, many membrane-associated signaling proteins, and the known arteriogenesis stimulating protein transforming growth factor beta-1 were increased after ECP therapy. In conclusion, ECP therapy increases platelet-derived MPs in patients with CAD and that the change in protein cargo of MPs is likely in favor of a pro angiogenic/arteriogenic property.

• **Alvaro N Gurovich and Randy W Braith. Enhanced external counterpulsation creates acute blood flow patterns responsible for improved flow-mediated dilation in humans. Hypertension Research advance online publication, 18 October 2012; doi:10.1038/hr.2012.169**

Enhanced external counterpulsation (EECP) is a FDA-approved treatment for patients with coronary artery disease and unstable angina. Although beneficial effects of EECP have been linked to central/cardiac adaptations, recent findings have shown peripheral/vascular effects. Here, we sought to determine EECP-induced blood flow patterns and their association with vascular function. The present study was designed to investigate endothelium-mediated arterial vasodilation changes after one 45-min session of either EECP or Sham EECP in 18 randomly assigned apparently healthy, young men (25±4 years). Brachial (b) and femoral (f) flow-mediated dilation (FMD) were assessed before and within 10 min after completing EECP or Sham. After 20 min of EECP, peak blood flow velocity (V) and brachial and femoral artery diameters (D) were recorded live for 2 min. In addition, a blood sample was drawn from the earlobe to determine hematocrit and then to calculate blood viscosity (μ) and density (ρ), Reynolds number (Re=V*D/μ), and endothelial shear stress (ESS=2μ*V/D). EECP increased retrograde shear stress and retrograde-turbulent blood flow in the femoral artery and antegrade-laminar shear stress in the brachial artery. fFMD was increased after EECP compared with Sham and baseline (fFMD=13.1±3.7 vs. 7.9±4.6% and 7.8±4.5%, respectively, P<0.05) and bFMD was increased after EECP compared with baseline (bFMD=10.6±4.8 vs. 7.0±3.5%, P<0.05). Despite different blood flow patterns. These results provide novel evidence that a single session of EECP-induced blood flow patterns improve endothelial function in peripheral muscular conduit arteries.
- **Wenhua Lin, Li Xiong, Jinghao Han, Thomas Wai Hong Leung, Yannie Oi Yan Soo, Xiangyan Chen, Ka Sing Lawrence Wong.** External Counterpulsation Augments Blood Pressure and Cerebral Flow Velocities in Ischemic Stroke Patients With Cerebral Intracranial Large Artery Occlusive Disease. *Stroke.* 2012;43:00-00.

**Background and Purpose:** External counterpulsation (ECP) is a novel noninvasive method used to improve the perfusion of vital organs, which may benefit ischemic stroke patients. We hypothesized that ECP may augment cerebral blood flow of ischemic stroke patients via induced hypertension.

**Methods:** We recruited ischemic stroke patients with cerebral intracranial large artery occlusive disease and healthy elderly controls into this study. Bilateral middle cerebral arteries of subjects were monitored using transcranial Doppler. Flow velocity changes before, during, and after ECP were, respectively, recorded for 3 minutes while continuous beat-to-beat blood pressure data were recorded. Cerebral augmentation index was the increase in percentage of middle cerebral artery mean flow velocity during ECP compared with baseline. Transcranial Doppler data were analyzed based on ipsilateral or contralateral to the infarct side. Results: ECP significantly increased mean blood pressure of stroke patients and controls. During ECP, middle cerebral artery mean flow velocities of stroke patients increased on both ipsilateral and contralateral sides when compared with baseline (ipsilateral cerebral augmentation index, 9.64%; contralateral cerebral augmentation index, 9%; both P<0.001), but there was no increase in difference between the 2 sides when compared with each other. Mean flow velocities of controls did not change under ECP. After ECP, blood pressure and flow velocity of stroke patients returned to baseline level. Conclusion: ECP provides a new method of cerebral blood flow augmentation in ischemic stroke by elevation of blood pressure. Flow augmentation induced by ECP suggests the improvement of cerebral perfusion and collateral supply from infarct ipsilateral and contralateral sides.


This study assessed the long-term efficacy of Enhanced External Counterpulsation (EECP) in Turkey (TR) patients initially and compared these results with the United States (US) in a real world setting. In this study, 2070 patients were treated and followed in the US and 82 patients were treated and followed in TR. The International EECP Patient Registry Phase I and II was initiated and coordinated at the University of Pittsburgh. The aim of the "registry" was to assess the outcomes of clinical trials in a real world setting. Another unique feature of this study was to enroll patients not only from university hospitals but also from private hospitals, educational hospitals, and treatment centers. TR patients had less diabetes, hypertension, and hyperlipidemia than US patients (p<0.01). TR patients also had a higher proportion of diastolic augmentation (p<0.001). Both groups showed a significant reduction in the severity of angina after 35h EECP course (p<0.001). Major Adverse Cardiac Events (MACE) rate (death, coronary artery bypass graft, percutaneous coronary intervention, myocardial infarction) was low in both groups during treatment (2.5% vs 2.7%). At 1 year follow up, 84% of TR and 76% of US patients had maintained the improvement of angina. In conclusion, patients presenting for EECP treatment from TR had different baseline profiles from US patients. However, despite the high risk baseline characteristics, both cohorts achieved similar reduction in angina. In the long term follow-up, the MACE rate was low and the improvement after EECP was sustained in most of the patients.


Enhanced external counterpulsation (EECP) is a noninvasive outpatient therapy, approved by the U.S. Food and Drug Administration in 1995, for the treatment of patients with coronary artery disease (CAD) and refractory angina pectoris who fail to respond to standard revascularization procedures and aggressive pharmacotherapy. The popular hypothesis is that EECP promotes coronary collateral growth and improves myocardial perfusion. However, this understanding of EECP is a theory and remains
unproven in randomized clinical trials. The purpose of this review is to integrate a recent series of studies by the authors and others that identify the extracardiac mechanisms by which EECP decreases angina episodes and nitrate usage while improving exercise tolerance in patients with symptomatic CAD. EECP creates significant increases in shear stimulus via pulsatile retrograde flow and antegrade flow in the femoral and brachi
al arteries, respectively. Moreover, we calculate that with a resting heart rate of 60 beats per minute, 35 one-hour EECP sessions cause approximately 150,000 hyperemic episodes (stimuli) in the arteries of both the lower and upper extremities. These chronic maneuvers increase release of nitric oxide from endothelial cells and thus cause vasodilation, with a delayed return of the reflected wave from the lower body to the heart and reduced wasted left ventricular pressure energy.


Improved pharmacological, invasive, and surgical therapies for cardiovascular diseases over the last few decades have led to an increase in life expectancy of individuals with angina. Despite treatment with multiple medications and invasive procedures, these patients remain symptomatic and functionally limited. Enhanced external counterpulsation (EECP) is a safe, noninvasive, well-tolerated, and clinically effective outpatient physical therapy for many patients with refractory angina. Numerous trials demonstrate positive clinical responses to EECP, including reductions in angina and nitrate use, increase in exercise tolerance, and enhanced quality of life. Several mechanisms are thought responsible for the clinical benefits of this therapy. Despite the marked success rates EECP achieves, the treatment remains largely unknown. This review will summarize the current evidence for the use of EECP and spark a better understanding of the potential role of this treatment.

- **Yang DY, Wu GF. Vasculoprotective properties of enhanced external counterpulsation for coronary artery disease: Beyond the hemodynamics. International Journal of Cardiology; E pub ahead of print, published online 07 May 2012**

A growing pool of evidence has shown that enhanced external counterpulsation (EECP) is a non-invasive, safe, low-cost, and highly beneficial therapy for patients with coronary artery disease. However, the exact mechanisms of benefit exerted by EECP therapy remain only partially understood. The favorable hemodynamic effects of EECP were previously considered as the primary mechanism of action. Nevertheless, recent advances have shed light on the shear stress-increasing effects of EECP which are vasculoprotective and antiatherosclerotic. EECP-induced endothelial shear stress increase may lead to improvement in endothelial function and morphology, attenuation of oxidative stress and inflammation, and promotion of angiogenesis and vasculogenesis. This review summarizes evidence of the potential mechanisms contributing to the immediate and long-term benefits of EECP, from the perspective of its shear stress-increasing effects.


Objective: Enhanced external counterpulsation (EECP) is a noninvasive treatment that is proven safe and effective in patients with coronary artery disease (CAD) and heart failure (HF). The aims of this study are to investigate the clinical effects of EECP therapy in patients with symptomatic CAD and chronic HF, and to find out an answer to the question: Does EECP therapy have any effect on the prognostic markers of HF? Methods: This study was designed as a prospective cohort study. A total of 68 consecutive patients with symptomatic CAD and chronic HF referred to EECP therapy were enrolled in this study between November 2007 and December 2010; 47 patients (39 males and 8 females, 65±7 years) have undergone EECP treatment, and 21 patients (20 males and 1 female, 62±10 years), who did not want to participate in the EECP program comprised the control-group. Statistical analysis was performed using t tests for dependent and independent samples, Mann-Whitney U test, Chi-square and Fischer exact tests. Results: EECP therapy resulted in significant improvement in post-intervention New York Heart Association functional class (p<0.001), left ventricular ejection (p<0.001), B-type natriuretic peptide levels (p<0.003), uric acid levels (p<0.05), free-T3/free-T4 ratio (p<0.034) and mitral annular E (p<0.05) velocity, compared
with baseline, a finding not evident in the control group. Conclusion: EECP treatment significantly improved clinical and some biochemical parameters, which are mostly prognostic markers in patients with symptomatic CAD and chronic HF.


Background: Lipid disorder causes vascular endothelial cell damage and contributes to the early development of dyslipidaemia-induced atherosclerosis. In vivo and in vitro, it has been found that increasing shear stress can improve endothelial function. Clinically, enhanced external counterpulsation (EECP) plays important roles in the treatment of coronary artery disease by promoting arterial shear stress. The present study aims to evaluate the effect of EECP on vascular endothelial function in porcine hypercholesterolemic model. Methods: Twenty-six hypercholesterolemic pigs were equally divided into EECP group (HC-EECP group) and control group (HC group). Shear stress of a right forearm superficial artery was measured during EECP in comparison with the basal physiological status in the HC-EECP group. Endothelial-dependent flow-mediated vasodilation (FMD) was applied to assess endothelial function. Serum high-sensitivity C-reactive protein (hs-CRP) levels were measured at indicated time points. Results: Endothelial shear stress was increased significantly during EECP treatment (p<0.001). Compared to HC group, hs-CRP decreased significantly by EECP at 18- and 36-h, respectively (p<0.05). FMD was improved significantly by EECP compared to that of HC group at 18 h (11.09 ± 5.63%) and at 36 h (11.42 ± 2.75%) post-EECP, p<0.05. Meanwhile, in animals of HC group, FMD was decreased from baseline 7.76 ± 3.70% to 6.75 ± 3.57% at 18 h and 5.07 ± 1.97% at 36 h, P<0.05. Conclusion: Long-term EECP can improve endothelial function partially by an increased endothelial shear stress in hypercholesterolemic porcine model. This implies that long-term EECP can be used as a complementary therapeutic strategy to prevent atherosclerosis in hypercholesterolemic patients.


Background: Enhanced external counterpulsation (EECP) has been reported to reduce blood pressure (BP) using clinic BP readings. The aim of this study was to assess the effect of a course of EECP on BP using ambulatory BP (ABP) measurements. Hypothesis: EECP has a lasting BP lowering effect. Methods: Patients referred for EECP due to refractory angina pectoris were consecutively included in the study. The ABPs were measured for 24 hours using a Spacelabs Ultralite 90217 device at 5 time points during the study period: 2 months before the EECP course, just before the EECP course, just after the EECP course, and at 3 and 12 months after EECP. Antihypertensive medication was held constant during the study period. Changes in BP were tested by repeated measures analysis. Results: Fifty patients were included in the study. The mean age was 63 years, and 72% were male. The Canadian Cardiovascular Society Angina Grading Scale class improved from a mean of 2.6 to 1.5. The mean daytime ABPs were 114/69, 114/70, 115/71, 114/70, and 116/71 mm Hg and the mean nighttime ABPs were 107/63, 108/63, 106/62, 108/63, and 107/62 mm Hg at 2 months before the EECP course, just before the EECP course, and at 3 and 12 months after EECP, respectively (all P > 0.10). Further, when controlling for quartiles of baseline ABP level, no significant change in ABP was found. Conclusions: Enhanced external counterpulsation treatment has no lasting effect on ABP.


Objectives: Enhanced external counterpulsation (EECP) is a non-invasive therapy with long-term anti-anginal effects offered to patients with refractory angina pectoris. The purpose of the present study was to investigate the effect of EECP on myocardial contractility measured as global longitudinal strain (GLS) during EECP treatment. Design: Patients with known refractory angina were enrolled by invitation and
Background & Aims: Enhanced external counterpulsation (EECP) is a non-invasive outpatient treatment used for angina pectoris. In patients with intractable angina who were symptomatic after medical and invasive strategies, several novel techniques are considered including EECP. In patients with refractory angina due to coronary anatomy specific information, CABG or PCI are also up despite anti-ischemic drug therapy are still symptomatic, other treatments including EECP is used. EECP produces an acute hemodynamic effect that is presumed to be similar to that produced by the invasive intra-aortic balloon pump: By applying a series of compressive cuffs sequentially from the calves to the thigh muscles upon diastole and rapidly deflating the cuffs in early systole, an increase in diastolic and decrease in systolic pressure is created. The purpose of this study was finding relationship between the therapeutic effects of enhanced external counterpulsation on refractory angina in patients, unsuitable for invasive interventions. Materials & Methods: In an Intermediary study, 50 consecutive patients (34 male, 16 female) were treated with EECP and followed for one year post treatment. Canadian cardiovascular society (CCS) class was analyzed, and medication and adverse clinical events were assessed prior to EECP, at the end of the treatment, and at 1 and 12 months thereafter. Any differences in background factors were recorded and analyzed. Results: the mean age of the 50 patients of this study was 62.18±8.67 years. A significant difference was found in score of life quality questionnaire between pre and after EECP treatment (p=0.01). Differences between EF pre and after treatment were significant (p=0.038). Differences between angina severity (CCS Score) pre and after EECP treatment were significant (p<0.001). Differences between Ischemia severity pre and after treatment were significant (p=0.044). There were no significant changes in Nitroglycerin usage pre and after treatment. Exercise duration significantly increased after Treatment (p=0.001). LVEDD and LVESD also significantly reduced (p=0.031, p=0.032). Exercise test duration one month after treatment was significantly increased compared with before treatment (p<0.001). There were no statistically significant difference in the amount of nitrates and other medications used before and after treatment in this study. Conclusion: this study demonstrated that EECP a useful method, effective and safe for patients with severe refractory angina pectoris resistant to drug therapy and aggressive measures such as PCI and CABG.

Objective: Functionally univentricular heart (FUH) anomalies are the leading cause of death from all structural birth defects. Total cavopulmonary connection (TCPC) is the last stage of the palliative surgical reconstruction with significant late hemodynamic complications requiring high-risk heart transplantation. Alternative therapeutic options for these critically ill patients are crucial. In Phase I, we investigated the effect of pulsatility of venous flow (VF) waveform on the performance of functional and “failing” Fontan (FF) patients based on conduit power loss. In phase 2, the effect of enhanced external counter pulsation on Fontan circulation flow rates is monitored. Methods: In phase 1, Doppler VFs were acquired from FF patients with ventricle dysfunction. Using computational fluid dynamics (CFD), hemodynamic efficiencies


of the FF, functional and in-vitro generated mechanically assisted VF waveforms were evaluated. In phase 2, Fontan circulation on sheep model was created and enhanced external counter pulsation (EECP) applied. Results: Variations in the pulsatile content of the VF waveforms altered conduit efficiency notably. High frequency and low amplitude oscillations lowered the pulsatile component of power losses in FF VF waveforms. The systemic venous flow, pulmonary artery and aorta flows increased by utilizing EECP. Conclusion: Our data highlighted the significance of VF pulsatility on energy efficiency inside SV circulation and the feasibility of VF waveform optimization. EECP assist in Fontan circulation can result in venous flow augmentation.


Background: The complicated concept of quality of life (QOL) has been considered as an important criterion for health outcomes in chronic diseases, such as heart disease, in recent years. The aim of this study was to evaluate the QOL of patients with angina pectoris after treatment with enhanced external counterpulsation (EECP). Methods: This quasi-experimental study was conducted on 64 patients with angina pectoris undergoing EECP who came to Shahid Chamran and Sina Hospitals in Isfahan. Sampling was performed by the convenient method. Data were collected using a questionnaire containing socio-demographic and clinical data. A standard questionnaire called 36-item Short-Form Health Survey was also used. Questionnaires were completed through interviews and phone calls in three stages (before, immediately and three months after the treatment). The results were analyzed using descriptive statistics (frequency, mean, and standard deviation) and analytical statistics (paired t-test and repeated measures test) in SPSS11.5. Results: The obtained results demonstrated that the majority of patients were men (59.4%) and aged 56-71 years. In addition, 57.8% had hypertension and 56.3% had hyperlipidemia. A history of myocardial infarction was found in 70.3% of the subjects and the familial history of coronary artery disease was detected in 73.4%. Although QOL evaluations showed improvements in all subscales immediately and three months after the treatment, the changes were not statistically significant in case of general health, role limitations due to physical problems and role limitations due to mental problems. Conclusions: Similar to previous research, this study showed QOL to improve in patients who undergo EECP. This improvement will remain stable three months after the treatment in all subscales. Therefore, EECP is an efficient noninvasive method in treating patients with angina pectoris and in developing their QOL.

2011


Mean platelet volume (MPV) is increased in chronic heart failure (CHF) and is an independent predictor of mortality in CHF patients. It is not known whether enhanced external counterpulsation (EECP) therapy leads to decrease MPV values or not. The purpose of this study was to examine the effects of EECP on platelet count and MPV values and to assess the influence of MPV on the risk of death and recurrent ischemic events in ischemic CHF patients. A total of 68 ischemic heart failure patients with CHF symptoms and refractory angina pectoris were included in the study, 47 consecutive patients (39 males and eight females) aged 44–82 years. Although follow-up period started after completion of EECP in treated patients, control group follow-up started at the end of 7-week treatment without EECP. All patients were monitored for a mean duration of 13W8 months (range, 1–36 months). The primary endpoints of the study were effects of EECP treatment on platelets after treatment period (7 weeks) and the recurrence of ischemic events. Secondary endpoint was cardiovascular death during the follow-up period. We observed a significant increase in platelet count and decrease in MPV levels (p<0.044 and p<0.004, respectively) in control group. There were no significant differences in platelet count and MPV levels in the EECP group (p>0.05). After the treatment period, New York Heart Association functional classification (2.60±0.75 vs. 1.72±0.68, p<0.001) and Canadian Cardiovascular Society functional classification of angina (2.50±0.90
Vasomedical: Synopses of Published EECP Papers 1992- Oct 2013

vs. 1.60±0.74, p<0.001) improved in patients with EECP treatment. In our study, we found that EECP therapy had a neutral effect on MPV values and platelet count.

- **WEI Hai-zhu. Effect of enhanced external counterpulsation on C-reactive protein and interleukin-6 in patients with coronary heart disease. Hainan, China Hainan Medical J. 2011; 22(3):56-57**

To investigate the effect of enhanced external counterpulsation (EECP) on reactive protein (CRP) and interleukin-6 (IL-6) in patients with coronary heart disease (CHD) and its mechanism. Methods: The serum level of reactive protein (CRP) and interleukin-6 (IL-6) in 80 cases with CHD and 20 normal controls were tested. Patients were divided into EECP group (40 cases) and medication group (40 cases). The serum concentrations of CRP and IL-6 in each group, before and after treatment were assessed and compared for the correlation analysis. Results: After 6 weeks and 3 courses EECP treatment, compared with the levels before treatment, the serum levels of CRP and IL-6 in patients with CHD, EECP group were lower significantly (P<0.05). Conclusion: EECP treatment may reduce IL-6 and CRP, which maybe has the protective the blood vessel endothelium function in patients with coronary heart disease.


Objective - To examine if the skin microvascular bed is altered and can be modified by enhanced external counterpulsation (EECP) in patients with chronic refractory angina. Methods - Twenty patients diagnosed with refractory angina were divided into EECP (n = 10) or no EECP (n = 10) groups. The data were compared to matched healthy subjects (n = 20). The cutaneous forearm microvascular blood flow was measured by Laser-Doppler flowmetry. The vascular responsiveness to iontophoretic administration of acetylcholine (ACh), sodium nitroprusside (SNP) and local skin warming were studied. Measurements of Canadian Cardiovascular Society (CCS)-class, blood pressure and plasma samples were registered. Results - EECP patients showed reduced CCS-class compared to no EECP (P<0.05). Both EECP and no EECP (p < 0.05) groups had decreased systolic blood pressure (SBP) as compared to SBP at baseline (p < 0.05). There was no difference in resting blood flow between the two refractory groups at baseline as well as after EECP and seven weeks of follow-up. Responses to heating, the responses to ACh and SNP in the cutaneous microcirculation were lower in both groups of refractory angina patients as compared to healthy subjects (P< 0.05). EECP patients corresponded positively to the treatment shown by reduced plasma level of soluble interleukin-2 receptor and CCS-class. Conclusions - Refractory angina patients have reduced responsiveness in their cutaneous microcirculation to ACh, SNP and heat compared to healthy subjects. Although EECP reduced the CCS-class, this effect was not associated with improvements in responsiveness of the cutaneous microcirculation.


In coronary artery disease patients, enhanced external counterpulsation (EECP) improves peripheral arterial function and nitric oxide (NO) bioavailability, which have been implicated in the pathogenesis of abnormal glucose tolerance (AGT). We sought to evaluate the effects of EECP on outcomes of arterial function, glucose tolerance, and skeletal muscle morphology in subjects with AGT. Methods and Results - Eighteen subjects with AGT were randomly (2:1 ratio) assigned to receive 34 either 7 weeks (35 1-hour sessions) of EECP (n = 12) or 7-weeks of standard care (control; n =35 6). Peripheral vascular function, biochemical assays, glucose tolerance, and skeletal muscle morphology were evaluated before and after EECP or control. EECP increased normalized brachial artery (27%) and popliteal artery (52%) flow-mediated dilation. Plasma nitrite/nitrate (NOx) increased (30%), 8-isoprostane-PGF-F2α, a marker of lipid peroxidation in the plasma, decreased (-23%). Fasting plasma glucose declined (-16.9 ± 5.4 mg/dL) and the homeostasis model assessment of insulin resistance (HOMA-IR) decreased (31%) following EECP.
Plasma glucose 120 minutes after initiation of oral glucose tolerance testing decreased (-28.3 ± 7.3 mg/dL) and the whole-body composite insulin sensitivity index (C-ISI) increased (21%). Vascular endothelial growth factor (VEGF) concentrations increased (75%) and vastus lateralis skeletal muscle biopsies demonstrated improvements in capillary density following EECP. No change was observed in cellular signaling pathways, but there was a significant increase GLUT-4 protein expression (47%) following EECP. Conclusions - Our findings provide novel evidence that EECP has a beneficial effect on peripheral arterial function and glucose tolerance in subjects with AGT.


Aims - The aim of this study was to compare acute hospital utilization and costs for patients with refractory angina pectoris undergoing spinal cord stimulation (SCS) versus enhanced external counterpulsation (EECP). Method - Seventy-three persons were included in this register study. The acute hospital utilization and costs for SCS and EECP were followed over a period from 12 months before treatment to 24 months after treatment using Patient Administrative Support in Skåne for publicly organized care. Results - SCS was significantly more expensive than EECP (p<0.001). Both SCS and EECP entailed fewer days of hospitalization for coronary artery disease in the 12-month follow-up compared with the 12 months preceding treatment. Patients treated with EECP showed an association between reduced hospital admissions and an improved Canadian Cardiovascular Society classification class compared with 1 year before treatment. A significant reduction in cost was seen in both the SCS group (P = 0.018 and p = 0.001, respectively) and the EECP group (p = 0.002 and p = 0.045, respectively) during 12 and 24 months of follow-up compared with before treatment. There were no significant differences between the groups for hospitalization days or admissions, including costs, at the different follow-ups. Conclusions - Cost-effective treatment modalities such as SCS and EECP are valuable additions to medical and revascularization therapy in patients with refractory angina pectoris. Pre-existing conditions and the patient’s preferences should be taken in consideration when clinicians choose between treatments for this group of patients.


Enhanced external counterpulsation (EECP) is a noninvasive technique for treatment of symptomatic coronary artery disease in patients not amenable to revascularization procedures. However, the mechanisms underlying the benefits of EECP remain unknown. We hypothesized that decreases in arterial stiffness and aortic wave reflection are a therapeutic target for EECP. Patients with coronary artery disease and chronic angina pectoris were randomized (2:1 ratio) to 35 1-hour sessions of EECP (n=28) or sham EECP (n=14). Central and peripheral arterial pulse-wave velocity and aortic wave reflection (augmentation index) were measured using applanation tonometry before, and after 17 and 35 1-hour treatment sessions. Wasted left ventricular pressure energy and aortic systolic tension–time index, markers of left-ventricular myocardial oxygen demand, were derived from the synthesized aortic pressure wave. Exercise duration, aninal threshold, and peak oxygen consumption were measured using a graded treadmill test. Central arterial stiffness and augmentation index were decreased after 17 and 35 sessions in the treatment group. Measurements of peripheral arterial stiffness were decreased after 35 sessions in the treatment group. Changes in aortic pressure wave reflection resulted in decreased measurements of myocardial oxygen demand and wasted left ventricular energy. No changes in central or peripheral arterial stiffness were observed in the sham group. Furthermore, measurements of exercise capacity were improved in the EECP group but unchanged in the sham group. In conclusion, EECP therapy decreases central and peripheral arterial stiffness, which may explain improvements in myocardial oxygen demand in patients with chronic angina pectoris after treatment.
John CK Hui, PhD

**Background** - Endothelial dysfunction is the earliest and most important factor in the pathogenesis of atherosclerosis. Inflammation has been shown to contribute to endothelial dysfunction. EECP has been shown to improve endothelial function besides symptomatic benefit in patients with refractory angina. In this patient population, depression has an unfavorable impact on mortality. We evaluated the effect of EECP on endothelial function, inflammatory markers of atherosclerosis and depression. Methods - Eight subjects (88%-male) were enrolled in EECP and four matched controls participated in the study. Endothelial dependent brachial artery flow mediated dilatation (FMD) was assessed, inflammatory markers were measured and the psychological effect of EECP was analyzed using Beck's-Depression-Scale before and after EECP. Results - The EECP group had a significant improvement in FMD after intervention (14.9 ± 3.97, p<0.00018) compared to control group (4.42 ± 2.02, p<0.1187). The EECP group also showed a significant increase in the anti-inflammatory marker interleukin-10 (mean 12.06 -pre to 22.66 -post), but no significant change in other pro-inflammatory markers (ICAM, E-Selectin, IL-6, CRP). EECP treatment showed an improvement in Becks-Depression-Scale after treatment (mean 18.13 -pre to 10.75 -post, p<0.0065). Conclusion - EECP group showed a significant improvement in endothelial function compared to the control. There was a significant increase in IL-10, which suggests one or more potential mechanisms of benefit. EECP also showed a significant improvement in symptoms of depression.


Background - In vivo observations of microcirculatory behavior during autoregulation and adaptation to varying myocardial oxygen demand are scarce in the human coronary system. This study assessed microvascular reactions to controlled metabolic and pressure provocation (bicycle exercise and external counterpulsation (ECP). Method - In 20 healthy subjects, quantitative myocardial contrast echocardiography and arterial applanation tonometry were performed during increasing ECP levels, as well as before and during bicycle exercise. Myocardial blood flow (MBF; ml·min⁻¹·g⁻¹), the relative blood volume (rBV; ml/ml), the coronary vascular resistance index (CVRI; dyn·s·cm⁻⁵/g), the pressure-work index (PWI), and the pressure-rate product (mmHg/min) were assessed. Results - MBF remained unchanged during ECP (1.08 ± 0.44 at baseline to 0.92 ± 0.38 at high-level ECP). Bicycle exercise led to an increase in MBF from 1.03 ± 0.39 to 3.42 ± 1.11 (p < 0.001). The rBV remained unchanged during ECP, whereas it increased under exercise from 0.13 ± 0.033 to 0.22 ± 0.07 (p< 0.001). The CVRI showed a marked increase under ECP from 7.40 ± 3.38 to 11.05 ± 5.43 and significantly dropped under exercise from 7.40 ± 2.78 to 2.21 ± 0.87 (both p < 0.001). There was a significant correlation between PWI and MBF in the pooled exercise data (slope: +0.162). During ECP, the relationship remained similar (slope: +0.153). Conclusions - Whereas physical exercise decreases coronary vascular resistance and induces considerable functional capillary recruitment, diastolic pressure transients up to 140 mmHg trigger arteriolar vasoconstriction, keeping MBF and functional capillary density constant. Demand-supply matching was maintained over the entire ECP pressure range.


EECP is used to stabilize the coronary circulation in patients with severe coronary artery disease when maximal medical therapy and/or invasive procedures have proven inadequate. This prospective observational study was done for a period of 12 months. 40 patients with angina and angiographically proven coronary artery disease, who met the inclusion and exclusion criteria was enrolled in this study.
Among 40 enrolled patients 30 (70%) patients completed their treatment. All the patients were in between 42 to 80 years age group. All patients required sublingual nitrate before started EECP treatment. But after completion of treatment, 75% patient required no nitrates. Who completed full course, 100% were improved their angina symptoms from class II, III, IV to class I. Overall 80% patients improved their quality of life. Those completed full course of treatment 100% patients improved their quality of life. EECP Heart therapy is now world-wide accepted alternative treatment option for those patients, who are not fit for surgery or any kind of interventional procedure and those developed heart failure.


Enhanced external counterpulsation (EECP) is a noninvasive circulatory assist device that has been recently emerged as a treatment option for refractory angina or left ventricular (LV) dysfunction. The aims of this study were to examine the effects of EECP on the electrocardiographic parameters and the heart rate variability indices of patients with the coronary heart disease and function class II-III angina resistant to medication. In a descriptive study, the patients who presented with sever angina at function class II-III were studied. Those meeting the inclusion criteria were invited to participate and provided informed consent. The standard enhanced external counterpulsation treatment (35 one-hour procedures 5-6 times a week) was done. Thirty minute ambulatory electrocardiographic monitoring and electrocardiogram before starting and at the end of treatment sessions were done. Data entry and analysis of data was done finally. Twenty five patients with mean age 68±9 year including 21(84%) men and 4(16%) women were enrolled in this study. Electrocardiographic parameters before and after treatment by EECP were not different statistically. Time domain indices of heart rate variability according to ambulatory monitoring findings were not changed significantly. Results of this study revealed that EECP didn’t improve the electrocardiographic and heart rate variability parameters of ischemic heart disease patients with refractory angina at function class II or III.

2010


Enhanced External Counterpulsation (EECP) has emerged as a promising non-invasive modality not only for patients with refractory angina pectoris (RAP) but also for patients with heart failure. To our knowledge, no published data exists in Pakistan about the benefits of EECP. We report on a case series of 16 consecutive patients undergoing EECP. All patients were either deemed not to be candidates for revascularization or had failed revascularization with RAP on optimal medical therapy. Data was collected regarding the coronary anatomy, clinical presentation, Pre and Post EECP Canadian Cardiovascular Society (CCS) class, nitrate use and 6-min walk test. Patients with severe peripheral vascular disease and arrhythmias were excluded. The mean age was 56 ± 11.1 years. Eight patients had 3-vessel disease, 4 post-CABG with occluded grafts and the rest with variable combination of coronary disease. Seven (44%) patients had Unstable Angina and 9 (56 %) had Stable Angina. The mean 6 min walk distance before EECP was 295 ± 148.60 meters and after EECP was 360 ± 102.12 meters (p = 0.013). The CCS class before and after EECP also showed significant improvement (p = 0.017). Sublingual nitroglycerine use also showed a positive trend after EECP. EECP was noted to be a safe and effective modality for patients with RAP with statistically significant improvement in measures of quality of life.


Objective - Enhanced external counterpulsation (EECP) is a non-invasive technique that has been shown to reduce the frequency and severity of angina pectoris. Little is known how EECP affects the blood
pressure. Methods - 153 patients with refractory angina were treated with either EECP or retained on their pharmacological treatment (reference group). Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and heart rate were measured pre- and post-treatment and at 12 months follow-up. Results - EECP treatment altered the blood pressure in patients with refractory angina pectoris. A decrease in the blood pressure was more common in the EECP group compared with the reference group. In the reference group, an increase in the blood pressure was more common. A correlation between a decrease in blood pressure after EECP treatment and a higher baseline MAP, SBP and DBP was seen.

No such correlation was seen in the reference group. The blood pressure response did not persist at 12 months follow-up. Conclusion - EECP treatment affects the blood pressure in patients with refractory angina pectoris. The decreased blood pressure may be a result of an improved exercise capacity, an improved endothelial function and vasoreactivity in general.


This is a review of current EECP status by a group in Bangladesh summarizing the historical background, principle of operation, and hemodynamics and its effects on endothelial function. Opening of collateral channels in the coronary vascular system after EECP treatment is presumed to be the mechanism to produce sustained benefit lasting several years. EECP is effective in treating refractory angina pectoris as demonstrated by the results of the randomized double blind, sham control multicenter study of EECP (MUST-EECP), and confirmed by the results from the International EECP Patients Registry (IEPR) which enrolled more than 7,500 patients in more than 100 international centers. Because EECP increases right ventricular filling pressure by augmenting venous returns during diastole, its use in patients with left ventricular dysfunction and heart failure would be contraindicated. However, EECP in the treatment of chronic heart failure has been reported in the randomized control PEIC study and IEPR. The 2005 ACC guidelines for the evaluation and management of chronic heart failure state that early trials of EECP therapy have been encouraging, more studies are needed to confirm its routine use. EECP has got clearance by the US Food and Drug Administration (FDA) to treat stable or unstable angina pectoris, and heart failure. It is not an alternative therapy to conventional revascularization; rather it could be regarded as an adjunctive therapy.


Background and Purpose: External counterpulsation (ECP) noninvasively improves myocardial and organ perfusion via diastolic augmentation. The effects on cerebral blood flow velocities (CBFV) and hemodynamics are controversial. In this study, the effect of active ECP treatment on CBF in healthy subjects was continuously measured. Methods: In 9 healthy volunteers (mean age 34.1± 8 11.1 years, 4 females), 20-min active ECP treatment was performed. CBFV in the middle cerebral artery were detected via transcranial Doppler. CBFV were registered continuously before, during and after ECP. The protocol was repeated twice. Results: At onset of ECP, immediate changes in CBFV were observed: peak diastolic blood flow velocities increased from baseline to treatment (63 vs. 76 cm/s; p≤ 0.001) and diastolic blood flow augmentation was maintained throughout ECP. Peak systolic (87 vs. 78 cm/s; p ≤ 0.001) and end-diastolic velocities (40 vs. 28 cm/s; p ≤ 0.001) decreased significantly, while mean CBFV maintained constant (59 vs. 58 cm/s; not significant). The pulsatility index and resistance index as indirect parameters for peripheral vascular resistance increased during ECP (pulsatility index 0.79 vs. 0.89, p≤ 0.001; resistance index 0.54 vs. 0.64; p≤ 0.001). Conclusions: ECP did not increase mean CBFV in healthy subjects even though peak diastolic CBFV were significantly augmented. Changes in CBFV and transcranial Doppler waveform characteristics suggest that the mean flow of the middle cerebral artery is maintained stable via cerebrovascular autoregulatory mechanisms.

Background: Mechanisms responsible for anti-ischemic benefits of enhanced external counterpulsation (EECP) remain unknown. This was the first randomized sham-controlled study to investigate the extracardiac effects of EECP on peripheral artery flow-mediated dilation. Methods and Results: Forty-two symptomatic patients with coronary artery disease were randomized (2:1 ratio) to thirty-five-one-hour sessions of either EECP (n=28) or sham EECP (n=14). Flow-mediated dilation of the brachial and femoral arteries was performed with the use of ultrasound. Plasma levels of nitrate and nitrite, 6-keto-prostaglandin F₁₀, endothelin-1, asymmetrical dimethylarginine, tumor necrosis factor-α, monocyte chemoattractant protein-1, soluble vascular cell adhesion molecule, high-sensitivity C-reactive protein, and 8-isoprostanate were measured. EECP increased brachial (+51% versus +2%) and femoral (+30% versus +3%) artery flow-mediated dilation, the nitric oxide turnover/production markers nitrate and nitrite (+36% versus +2%), and 6-keto-prostaglandin F₁₀ (+71% versus +1%), whereas it decreased endothelin-1 (-25% versus +5%) and the nitric oxide synthase inhibitor asymmetrical dimethylarginine (-28% versus +0.2%) in treatment versus sham groups, respectively (all P<0.05). EECP decreased the proinflammatory cytokines tumor necrosis factor-α (-16% versus +12%), monocyte chemoattractant protein-1 (-13% versus +0.2%), soluble vascular cell adhesion molecule-1 (-6% versus +1%), high-sensitivity C-reactive protein (-32% versus +5%), and the lipid peroxidation marker 8-isoprostanate (-21% versus +1.3%) in treatment versus sham groups, respectively (all P<0.05). EECP reduced angina classification (-62% versus 0%; P<0.001) in treatment versus sham groups, respectively. Conclusions: Our findings provide novel mechanistic evidence that EECP has a beneficial effect on peripheral artery flow-mediated dilation and endothelial-derived vasoactive agents in patients with symptomatic coronary artery disease.

PG Jørgensen, J Lindberg, O May. Toxic shock syndrome: A rare complication to enhanced external counterpulsation, Can J Cardiol 20 10;26(10) e351.e3 52.

A case with a previously unknown complication - toxic shock syndrome (TSS) that occurred twice in an EECP treated patient is described. A 64-year-old man with a long history of ischemic heart disease was admitted with a rapid onset of fever, confusion and hypotension. On admission, his blood pressure was 100/65 mm Hg, but soon dropped to 75/40 mm Hg in spite of fluid replacement. Broad-spectrum antibiotics and vasopressor therapy were started, and the blood pressure normalized. Septic shock was suspected and the patient. On the fourth day of admission, TSS was diagnosed and clindamycin was added to the antibiotic regimen. The symptoms prompting hospitalization started 12 h after the first session in a planned EECP course. After a few days patient improved and discharged After two months, the patient started another course of EECP. Once again, a few hours after the first session, he developed fever, confusion, shock, and demarcated erythema on his right lower extremity. Treatment with broad -spectrum antibiotics, including clindamycin was started and the condition improved after a few hours of treatment. Six months after discharge, the patient still had severe angina and was eager to resume EECP. Although a toxin-producing microorganism could not be isolated, except for the group B streptococcus, it was decided that the patient would be given prophylactic antibiotics with clindamycin during the entire EECP course. No further complications were observed. Toxic shock syndrome initially resembles the state of septic shock. Early recognition of the syndrome and initiation of therapy is of vital importance to prevent rapid progression and a possibly fatal outcome. Awareness of this condition among cardiologists offering EECP is essential.


Background: Enhanced external counterpulsation (EECP) is associated with improvement in endothelial function, angina and quality of life in patients with symptomatic coronary artery disease, although the mechanisms underlying the observed clinical benefits are not completely clear. The purpose of this study was to examine the effects of EECP on circulating haematopoietic progenitor cells (HPCs) and
endothelial progenitor cells (EPCs) in patients with refractory angina. We compared HPC and EPC counts between patients scheduled for EECP and patients with normal angiographic coronary arteries, with and without coronary endothelial dysfunction. We hypothesized that an increase in circulating bone marrow derived progenitor cells in response to EECP may be part of the mechanism of action of EECP. Methods: Thirteen consecutive patients scheduled to receive EECP treatment were prospectively enrolled. Clinical characteristics were recorded and venous blood (5 ml) was drawn on day 1, day 17, day 35 (final session) and one month post completion of EECP therapy. Buffy coat was extracted and HPCs and EPCs were counted by flow cytometry. Results: Median Canadian Cardiovascular Society (CCS) angina class decreased and Duke Activity Status Index (DASI) functional score increased significantly (both, p<0.05) in response to EECP, an effect that was maintained at one month after termination of treatment. Flow cytometric analysis revealed an accompanying significant increase in CD34+, CD133+ and CD34+, CD133+ CPC counts over the course of treatment (pb0.05). DASI scores correlated significantly with CD34+ (R=0.38 p=0.02), CD133+ (R=0.5, p=0.006) and CD34+, CD133+ (R=0.47, p=0.01) CPC counts. Conclusion: This study shows that HPCs, but not EPCs are significantly increased in response to EECP treatment and correlate with reproducible measures of clinical improvement. These findings are the first to link the functional improvement observed with EECP treatment with increased circulating progenitor cells.


This is a review paper on the hemodynamic effects during EECP with comparison to intra-aortic balloon pump (IABP) whenever possible. Early external counterpulsation (ECP) using hydraulic activator with single chamber water filled leg compression bags failed to produce effective systolic unloading, increased oxygen consumption, whereas IABP lower systolic pressure, lower oxygen consumption. The acute hemodynamic effects of the improved design pneumatic-driven sequential inflation EECP have been assessed by various authors both noninvasively by finger plethysmography, thoracic electrical bioimpedance, echocardiography, and radial tonometry as well as invasively by right heart catheterization, radial artery catheterization, intracoronary pressure and Doppler flow, and simultaneous right and left heart catheterization. In patients with uncomplicated acute myocardial infarction, Taguchi et al (see 2000 synopses) demonstrated the hemodynamic effects of ECP were similar to those of IABP for diastolic augmentation and systemic vascular resistance with higher increase in right atrial pressure, pulmonary capillary wedge pressure, and cardiac index, suggesting that EECP increases venous return, raises cardiac preload, and increased cardiac output. In patients referred for cardiac catheterization, Michaels and colleagues (see 2002 synopses) provided solid evidence using intracoronary, central aortic and left ventricular pressure and intracoronary Doppler flow that the hemodynamic effects of EECP are comparable to IABP. The clinical implications of these hemodynamic effects suggested that higher ratios of diastolic augmentation to systolic unloading are associated with improved short or long-term clinical outcomes. In patients with heart failure, it is important to balance any increased venous return with systolic unloading, which is usually achieved with high cuff pressure.


There are four stages of EECP development. Phase 1 Physiological concepts and innovation idea: EECP starts with two ideas: Kantrowitz and Kantrowitz first described the principle of diastolic augmentation (DA) to increase coronary blood flow in 1953 and Sarnoff and colleagues described that myocardial workload is proportional to the pressure generated by the left ventricular and its contraction time. Then in 1957 Birtwell proposed to design a device that can synthesize the two concepts. Phase 2 Technical development, from concept to design: in 1963 Soroff and coworkers described an actuator with a chamber to receive arterial blood via a cannulation of the descending aorta to withdraw a volume of blood during systole and returning the blood during diastole. Then in late 1960s a hydraulic actuator consisted of a rigid outer case enclosing a single pant like bag filled with water put around the lower extremities of the patient. Pressures were applied and released by pumping water in and out of the bag in synchronization the cardiac cycle. In 1976 Zheng ZS and colleagues in China developed a pneumatic system with six cuffs wrapped around the calves and lower and upper thighs. The device was named enhanced external counterpulsation (EECP). Phase 3 Clinical evidence of safety and effectiveness: from
1960s to 1970s, there were many papers in the treatment of AMI and cardiogenic shock in the United States, with definitive hemodynamic effects but mixed clinical results. During the 1980s to 1990s there were numerous case reports in China, treating many different types of ischemic diseases. Unfortunately many of these case reports had no control groups, lack in strict criteria in selecting patients. Since then there were more than 150 papers published with approximate 200 presentations in major scientific meetings. There were two major randomized control studies, the MUST-EECP for angina pectoris patients and the PEECH trial for heart failure patients. In addition, there were two registries with 5,000 and 3,000 patients. Phase 4 Society adaptation and acceptance: It is important for government to invest in research and encourage reasonable coverage in therapies that can save health care cost. EECP has been shown to reduce hospitalization of heart failure patients. With recent findings on the mechanisms of action, EECP may be effective in the prevention of cardiovascular disease progression and reduction of health care cost. These four phases do not occur in series but constantly interact and feedback on each other, evolving on their way to maturity.


The link between risk factors leading eventually cardiovascular disease including heart failure is endothelial dysfunction. EECP increases velocity of blood flow and shear stress acting on the endothelial cells, stimulating release of endothelial nitric oxide synthase (eNOS), increases release of vasodilator nitric oxide (NO) and suppresses vasoconstrictor endothelin E-1, thereby improving flow mediated vasodilatation, a measure of endothelial function. EECP also lowers arterial stiffness, systolic and pulse pressure leading to reduction of cardiac workload and myocardial oxygen demand. It has been documented EECP also stimulates endothelium to release vascular endothelial growth factor (VEGF), and together with the mechanical pressure gradient generated during EECP, promotes coronary collateral flow index, coronary fractional flow reserve and reduces microcirculatory resistance. EECP also decreases circulating levels of inflammatory cytokines such as tumor necrosis factor –α, monocyte chemoattractant protein-1, C-reactive protein, mitogen-activated protein kinase-p38 and nuclear factor kappa β. EECP therapy has also been documented to activate endothelial progenitor stem cells to replace and repair endothelium apoptosis thereby enhance endothelial function and inhibiting intimal hyperplasia and proliferation and migration of smooth muscle cell, slowing down atherosclerotic process and progression of cardiovascular disease.


There is accumulating evidence that ECP therapy may improve cerebral blood flow (CBF). A study showed that the mean carotid flow velocity integral increased by 22% during ECP, with an average peak carotid diastolic flow velocity of 56 cm/sec, which is 75% as high as the systolic wave. There were two randomized controlled studies demonstrated ECP improved the average CBF from 45.7±6.0 ml/100 g/min to 55.6±6.0 ml/100 g/min in the ECP treated group, whereas no significant change was found in the control group; and a second study with 29 (72.5%) patients in the ECP group versus 22(55%) patients in the control group had a favorable clinical outcome. Studies also have shown significant decrease in hematocrit, fibrinogen level and plasma viscosity after ECP, which may be associated with the improvement in cerebral circulation. More importantly, these changes in biomarkers were accompanied with a clinical improvement. A recent randomized, crossover, assessment-blinded pilot study demonstrated ECP is safe and feasible for stroke patients with large artery disease. 50 patients were randomized to either early (ECP week 1-7 and no ECP week 8-14) or late group (no ECP week 1-7 and ECP week 8-14). At end of week 7, there was a significant change in NIHSS (early 3.5 vs late 1.9; p=0.042). ECP was associated with a favorable trend of change in NIHSS of 2.1 vs 1.3 for non-EECP (p=0.061) after adjusted for treatment sequence. At week 14, a favorable functional outcome was found in 100% of early group patients compared to 76% in the late group (P=0.022). Thus, ECP therapy holds great promise for the treatment of ischemic stroke and more has to be learned about the mechanism responsible for its clinical benefits. In the future, it is important to identify the subtype of ischemic stroke patients whom may benefit most from ECP treatment.

Enhanced External Counterpulsation (EECP) has emerged as a promising non-invasive modality not only for patients with refractory angina pectoris (RAP) but also for patients with heart failure. To our knowledge, no published data exists in Pakistan about the benefits of EECP. We report on a case series of 16 consecutive patients undergoing EECP. All patients were either deemed not to be candidates for revascularization or had failed revascularization with RAP on optimal medical therapy. Data was collected regarding the coronary anatomy, clinical presentation, Pre and Post EECP Canadian Cardiovascular Society (CCS) class, nitrate use and 6-min walk test. Patients with severe peripheral vascular disease and arrhythmias were excluded. The mean age was 56 ± 11.1 years. Eight patients had 3-vessel disease, 4 with post-CABG with occluded grafts and the rest with variable combination of coronary disease. Seven (44%) patients had Unstable Angina and 9 (56 %) had Stable Angina. The mean 6 min walk distance before EECP was 295 ± 148.60 meters and after EECP was 360 ± 102.12 meters (p = 0.013). The CCS class before and after EECP also showed significant improvement (p = 0.017). Sublingual nitroglycerine use also showed a positive trend after EECP. EECP was noted to be a safe and effective modality for patients with RAP with statistically significant improvement in measures of quality of life.


Objective: To evaluate the true magnitude of benefit from enhanced external counterpulsation (EECP) by determining the effect of EECP on Canadian Cardiovascular Society (CCS) angina class in patients with chronic stable angina. Design: Meta-analysis of 13 prospective studies that evaluated patients with stable angina and reported adequate data on CCS angina class. Patients: A total of 949 adult patients with stable angina who underwent EECP treatment. Measurements and Main Results: A systematic literature search of studies published between 1950 and February 2009 was performed. Studies were included for meta-analysis if they were reported in the English language, included human subjects, had a prospective study design, and reported adequate data on CCS angina class. The EECP treatment consisted of 35 sessions-1 hour/day, 5 days/week, for 7 weeks. Improvement in angina class was reported as the weighted proportion of patients improving by at least one CCS class from before to after EECP treatment. Heterogeneity was assessed by performing subgroup analyses and using the Cochran Q statistic. Publication bias was assessed by inspection of funnel plots and the Egger bias statistic. Among the 13 studies incorporating 949 patients, angina class was reduced by at least one CCS score in 86% of the patients (95% confidence interval 82–90%, Q statistic p=0.008. Inspection of funnel plots showed some asymmetry, but the Egger bias statistic showed no publication bias (p=0.97). Conclusion: The results of our meta-analysis call for further long-term studies to determine the place of EECP therapy in the management of chronic stable angina. Currently, EECP therapy should be considered for patients with stable angina who are refractory to or not suitable for invasive therapy and/or medical management.


This is a review paper by a group of Indian EECP physicians documenting the mechanism of action and clinical outcome in patients with refractory angina and heart failure. Specifically this review provides a list of patients who will benefit from EECP: patients whom PTCA or CABG is not contemplated, patients with ischemic or idiopathic cardiomyopathy and patients with cardiac syndrome X (microvascular angina). This review also outlines some interesting papers published in India which reconfirm the improvement in myocardial perfusion and improvement in LV ejection fraction in the Indian population. These effects were seen in both patients with refractory angina and ischemic Cardiomyopathy. The data from the Indian patient EECP registry which tracks both the subjective and objective improvements shown that the improvement in LV ejection fraction is predominantly due to reduction in end systolic volume.
demonstrating improvement in LV contractility after EECP therapy. In another interesting study a short course 10 sessions of EECP therapy done prior to performing high risk CABG has shown improvement in myocardial perfusion and LV function. In addition, patients in this study who went on to have CABG have decreased complication during and after their surgery. This result demonstrates EECP may have beneficial effect in surgical outcome in this group of patients. This hypothesis needed to be tested in large randomized study. The review concludes that enhanced external counterpulsation is a proven non-invasive treatment option to be considered for patients with refractory angina and HF. EECP therapy is the only mechanical therapy, which has shown not only effective in improving myocardial supply in angina patients but also shown to improve endothelial function and decrease the myocardial demand. Due to its effect on vascular endothelium and microvascular circulation it can also be used to treat patients with microvascular angina or cardiac syndrome X. Refractory angina and HF utilizes increase health care cost due to repeat hospitalization and revascularization. EECP is the most cost effective treatment for this selected group of patients. The utilization of EECP in earlier stage of CAD will be an attractive option and its needs further evaluation. The treatment is safe in patients with stable angina pectoris with mild to moderate LV dysfunction.


This is a case report of a 57-year-old woman admitted to the local hospital due to chest pain in 2001. Coronary angiography (CA) showed proximal subocclusion of the first diagonal branch (D1), significant stenosis in the LAD. Percutaneous coronary intervention (PCI) without stent was performed on D1 and a bare metal stent on the LAD. In the following two years, patient was admitted frequently due to chest pain in spite of normal perfusion, biochemical markers and optimal medications including beta-blockers, Ca antagonists, nitrates, ACE-inhibitors and statins. Several CA were performed showing no occlusion. It was concluded that patent suffered from Prinzmetal’s angina and beta-blockers were withdrawn. Despite optimal medical therapy, the patient was admitted numerous times with chest pain and ST-elevation in the inferior ECG leads which was promptly reversed by administration of nitroglycerin intravenously. Cypher stents were implanted in the RCA but spasms continued. In 2005, the patient had a thoracic sympathectomy performed, but this was also without effect on the chest pain. In 2006, the patient completed a course of EECP consisting of 5 hourly sessions each week in 7 weeks. Prior to EECP, the patient self injected nitroglycerin 15-20 mg intravenously in a Broviac catheter every three hours around the clock, but after EECP the nitroglycerin consumption was reduced to only 6 mg taken on demand. Quality of life was significantly improved and angina was reduced from Canadian Cardiovascular Society class IV to I. During the two years prior to EECP the patient was admitted to hospital due to chest pain 81 times, nut in the two years following EECP she was only hospitalized twice due to chest pain. The clinical improvement found in this patient is most likely due to the improved endothelial function induced by EECP. To our knowledge this is the first case report demonstrating the effect of EECP on Prinzmetal’s angina pectoris.


Symptomatic coronary artery disease (CAD) and heart failure (HF), either of ischemic or nonischemic etiology, are common medical problems. Despite optimal medical treatment and improved revascularization techniques, a significant number of patients are not successfully managed. Among the non-pharmacological, alternative, non-invasive treatments suggested for these patients, enhanced external counterpulsation (EECP) is considered the most effective one. EECP administered in an outpatient setting, consists of three pneumatic cuffs applied to each of the patient’s legs that are sequentially inflated and deflated synchronized with the cardiac cycle. Numerous clinical trials have shown that EECP is safe and effective in patients with ischemic heart disease, with or without left ventricular dysfunction, improving their quality of life, EECP appears to be beneficial as an adjunctive therapy in patients with HF of any etiology. Cardiac syndrome X has been shown to be effectively treated with EECP. Research in EECP expanded in its potential use for entities other than heart disease. More trials are necessary including sham-controlled trials, to further establish EECP among medical society...

**Objective:** Shear stress may be the most crucial local factor affecting atherogenesis. The present study investigated the effect of exposure to increased shear stress promoted by enhanced external counterpulsation (EECP) on the progression of atherosclerosis and the underlying inflammation-related molecular mechanisms in a porcine model of hypercholesterolemia. **Methods and Results:** Hypercholesterolemic pigs were subjected to a 7-week EECP intervention while being fed a high-cholesterol diet. EECP resulted in a 34.38% increase of mean wall shear stress and a significantly lower pulsatility index in the brachial artery. The animals receiving EECP showed a marked reduction in atherosclerotic lesion size in the coronary artery and abdominal aorta compared with the hypercholesterolemic control group, associated with a decrease in macrophage accumulation. The expression of a set of genes involved in inflammation (including C-reactive protein [CRP], complement 3a, vascular cell adhesion molecule-1 [VCAM-1], and inducible nitric oxide synthase), mitogen-activated protein kinase (MAPK)-p38 phosphorylation, and nuclear factor-κB (NF-κB) activation, was attenuated. **Conclusion:** These findings suggested that long-term EECP exerts a retarding effect on atherosclerosis by downregulating proinflammatory gene expression. The underlying mechanisms are related to chronic exposure to increased pulsatile shear stress promoted by EECP; this exposure suppresses the over-activation of the MAPK-P38/NF-κB/VCAM-1 signaling pathway induced by hypercholesterolemia.


Study Design: Clinical trial of patients with rotational vertebrobasilar insufficiency (VBI) resulting from cervical spondylosis. **Objective:** To investigate the effectiveness of enhanced external counterpulsation (EECP) and traction therapy for these patients. **Summary of Background Data:** EECP would reduce arterial stiffness and vascular resistance, and increase regional blood flow of vertebral arteries, thus may ameliorate symptoms in these patients. **Methods:** One hundred sixty-three patients who were clinically suspected rotational VBI caused by cervical spondylosis were enrolled in this study. They were randomly allocated into 3 groups: EECP + traction, EECP, and traction group. All patients and 50 healthy volunteers received transcranial color Doppler examination of the vertebral artery and basilar artery in both a neutral cervical spine position and a rotational position. **Results:** Within 3 days after treatment, 47 (84%) patients in EECP + traction group, 32 (61%) patients in EECP group, and 8 (15%) patients in traction group achieved successful outcomes, while at 3 months follow-up, 45 (80%) patients in EECP + traction group, 34 (64%) in EECP group, and 3 (6%) in traction group achieved successful outcomes. With head rotation, the percentage of reduction of blood flow velocities of the vertebrobasilar artery (VBA) in patients was much greater than that of the healthy volunteers (p < 0.01). After treatment, rotational blood flow velocity reduction percentage of VBA in each treatment group was much lower than that of each group before treatment. EECP + traction group experienced the greatest decrease of rotational blood flow velocity reduction percentage of VBA, while EECP group experienced second greatest. **Conclusion:** EECP and traction therapy can relieve the symptoms of rotational VBI, improve the rotational reduction of vertebrobasilar blood flow, and reduce the increased arterial impedance.


Enhanced external counterpulsation (EECP) is used for the treatment of severe angina and heart failure in patients who are not candidates for revascularization. The clinical benefits of EECP extend well beyond the time period of any hemodynamic effects, but the cause of this prolonged effect is not understood. The prolonged clinical benefits suggest EECP could be a regenerative therapy. This study was performed to determine whether EECP increased circulating hematopoietic progenitor cells (HPCs) or endothelial progenitor cells (EPCs) and thus be a possible regenerative therapy. The proposed mechanism of the
increase in regenerative circulating stem cells is the enhanced shear forces induced on the endothelial boundary by the flow reversal produced by the sequential inflation of the pneumatic cuffs during EECP therapy. Nine patients were recruited from those referred for EECP. There were 8 men and 1 woman with a mean age 70.2 ± 10.2 years. All patients had limiting angina (Canadian Cardiovascular Society class II or greater), were receiving appropriate medical therapy and were not considered candidates for revascularization. There were no significant differences in the counts for either progenitor cell line comparing the values for the samples obtained 5-7 days before treatment with the values obtained immediately before the first treatment. The total number of cells increased progressively during the 4 weeks of therapy. After 4 weeks, there was a significant increase in EPCs (p = 0.014 compared with the baseline value). Likewise, the number of HPCs also increased significantly (p=0.008 compared with baseline) during treatment. Before EECP, the median CCS class was 3.0 and decreased to 1.5 after 4 weeks of therapy (p<0.01). In conclusion, the present study demonstrates an increase in progenitor cells during EECP therapy in patients with severe coronary artery disease. The mechanism whereby EECP causes this increase is unknown, but this observation could provide an explanation for the angiogenesis and improvements in left ventricular function observed with EECP and the long-lasting benefits following EECP therapy. By increasing circulating progenitor cells EECP could be considered a regenerative therapy and further proof of this concept may be warranted in the treatment of other degenerative diseases including vascular ulcers, peripheral neuropathy, Parkinson's disease, stroke, and myocardial infarction. Other methods of mechanically increasing circulating stem cells could also be investigated.

2009


BACKGROUND: Endothelial dysfunction contributes to the manifestation of stable and unstable coronary syndromes in patients with established coronary artery disease (CAD). Enhanced external counterpulsation (EECP) is a noninvasive therapeutic modality for patients with CAD, non responsive to medical and/or surgical treatment. The aim of this research was to determine the long-term effect of EECP on endothelial function via releasing angiogenic factors, NO (nitric oxide) and VEGF (vascular endothelial growth factor), in patients with CAD. METHODS: The study was performed on 19 consecutive patients with ischemic coronary artery disease. All subjects were treated with EECP 1-h per day, 5 days a week, over 7 weeks (totally 35 h). Serum level of VEGF and nitrite (stable NO metabolite) concentration was measured before EECP, after 24th day, at the end of course (35th day), and at 1 and 3 months after completion of EECP treatment. RESULTS: After 35 hours of EECP, there was a trend toward increase (31.5 ± 14.7%) in nitrite level compared with baseline (11.12 ± 3.17 vs 9.65 ± 1.36 mg/l) but it wasn’t significant. Results of 1and 3 month follow-up after treatment showed that, the nitrite levels significantly increased compared with the baseline. During the course of EECP therapy, plasma VEGF levels increased progressively. Significant increase in plasma levels of VEGF were begun from second sampling session of our study (24th day) and reached to maximum 3 month after EECP therapy. CONCLUSION: In this prospective study that assessed the effects of EECP on plasma nitrite and VEGF levels, it has been demonstrated that EECP progressively increases nitrite and VEGF levels during the course of therapy. These significant changes continued 3 months after EECP therapy.


Background: The efficacy of external counterpulsation (ECP) on coronary collateral growth has not been investigated in a randomized controlled study. Objective: To test the hypothesis that ECP augments collateral function during a 1 min coronary balloon occlusion. Patients and methods: Twenty patients with chronic stable coronary artery disease were studied. Before and after 30 h of randomly allocated ECP (20 90 min sessions over 4 weeks at 300 mm Hg inflation pressure) or sham ECP (same setting at 80 mm Hg
inflation pressure), the invasive collateral flow index (CFI, no unit) was obtained in 34 vessels without coronary intervention. CFI was determined by the ratio of mean distal coronary occlusive pressure to mean aortic pressure with central venous pressure subtracted from both. Additionally, coronary collateral conductance (occlusive myocardial blood flow per aorto-coronary pressure drop) was determined by myocardial contrast echocardiography and brachial artery flow-mediated dilatation was obtained. Results: CFI changed from 0.125 (0.073; interquartile range) at baseline to 0.174 (0.104) at follow-up in the ECP group (p=0.006), and from 0.129 (0.122) to 0.111 (0.125) in the sham ECP group (p=0.14). Baseline to follow-up change of coronary collateral conductance was from 0.365 (0.268) to 0.568 (0.585) ml/min/100 mm Hg in the ECP group (p=0.072), and from 0.229 (0.212) to 0.305 (0.422) ml/min/100 mm Hg in the sham ECP group (p=0.45). There was a correlation between the flow mediated dilatation change from baseline to follow-up and the corresponding CFI change (r=0.584, p=0.027). Conclusions: ECP appears to be effective in promoting coronary collateral growth. The extent of collateral function improvement is related to the amount of improvement in the systemic endothelial function.


Peripheral arterial disease (PAD) is common in patients with severe coronary artery disease (CAD) and is considered a relative contraindication to external enhanced counterpulsation (EECP), but there are no data that define the efficacy and safety of EECP in patients with PAD. The International EECP Patient Registry (IEPR) was used to compare initial post therapy and 2-year follow-up clinical outcomes and adverse event rates in patients with and without PAD. From January 2002 to October 2004, 2126 patients were enrolled in the IEPR, of whom 493 (23%) had a history of PAD. Immediately following EECP, the reduction in angina (≥ 1 Canadian Cardiovascular Society class) was similar in patients with and without PAD (76.6% vs 79.0%, p = 0.27) as was improvement in the Duke Activity Score Index (DASI) score (+4.7% vs +6.1%, p < 0.001). Both angina reduction and DASI score improvement were sustained at 2 years. PAD patients discontinued EECP more frequently (12.0% vs 8.5%, p < 0.05), but lower extremity ulceration did not occur more frequently in patients with PAD (3.7% vs 2.7%, p = 0.26). Rates of death (17.1% vs 8.6%, p < 0.01) and myocardial infarction (9.5% vs 5.0%, p < 0.01) were, as expected, higher in patients with PAD compared to patients without PAD at 2 years. In conclusion, while PAD patients constitute a high-risk cohort with known higher adverse event rates, EECP led to similar short- and long-term improvements in angina and quality of life for individuals with PAD compared to those without PAD.


The prevalence of refractory angina in the United States is 600,000 to 1.8 million. Improved pharmacological, invasive, and surgical therapies for cardiovascular diseases during the last few decades have led to an increase in life expectancy of such individuals. Despite treatment with multiple medications and invasive procedures, these patients remain symptomatic and functionally limited. Enhanced external counterpulsation (EECP) is a safe, noninvasive, well tolerated, and clinically effective outpatient physical therapy for many patients with refractory angina. Numerous trials demonstrate positive clinical responses among at least 80% of patients undergoing EECP, including reductions in angina and nitrate use, increases in exercise tolerance, and enhanced quality of life. Several mechanisms, including the promotion of collateral blood flow, improvement in endothelial function, reduction in inflammation, and the production of peripheral training effects similar to exercise, are thought to be responsible for the clinical benefits of this therapy. Despite the marked success rates EECP achieves with appropriately selected patients who have end-stage coronary artery disease, the treatment remains largely unknown, particularly among physiatrists. This review will summarize the current evidence for the use of EECP and spark a better understanding of the potential role of this treatment in cardiac rehabilitation.
Background Arteriogenesis (collateral artery growth) is nature’s most efficient rescue mechanism to overcome the fatal consequences of arterial occlusion or stenosis. The goal of this trial was to investigate the effect of external counterpulsation (ECP) on coronary collateral artery growth. Materials and methods A total of 23 patients (age 61 ± 2.5 years) with stable coronary artery disease and at least one hemodynamic significant stenosis eligible for percutaneous coronary intervention were prospectively recruited into the two study groups in a 2 : 1 manner (ECP : control). One group (ECP group, n = 16) underwent 35 1-h sessions of ECP in 7 weeks. In the control group (n = 7), the natural course of collateral circulation over 7 weeks was evaluated. All patients underwent a cardiac catheterization at baseline and after 7 weeks, with invasive measurements of the pressure-derived collateral flow index (CFIp, primary endpoint) and fractional flow reserve (FFR). Results In the ECP group, the CFIp (from 0.08 ± 0.01 to 0.15 ± 0.02; p<0.001) and FFR (from 0.68 ± 0.03 to 0.79 ± 0.03; p=0.001) improved significantly, while in the control group no change was observed. Only the ECP group showed a reduction of the Canadian Cardiovascular Society (CCS, p=0.008) and New York Heart Association (NYHA, p<0.001) classification. Conclusion In this study, we provide direct functional evidence for the stimulation of coronary arteriogenesis via ECP in patients with stable coronary artery disease. These data might open a novel noninvasive and preventive treatment avenue for patients with non-acute vascular stenotic disease.

Background Stimulation of collateral artery growth is a promising therapeutic option for patients with coronary artery disease. External counterpulsation is a non-invasive technique suggested to promote the growth of myocardial collateral arteries via increase of shear stress. The Art.Net.2 Trial tests invasively and functionally for the first time the hypothesis whether a treatment course with external counterpulsation (over 7 weeks) can induce the growth of myocardial collateral arteries. Methods This study is designed as a prospective, controlled, proof-of-concept study. Inclusion criteria are (1) age 40 to 80 years, (2) stable coronary disease, (3) a residual significant stenosis of at least one epicardial artery and (4) a positive ischemic stress-test for the region of interest. As primary endpoint serves the pressure-derived collateral flow index (CFIp), the invasive gold-standard to assess myocardial collateral pathways. CFIp is determined by simultaneous measurement of mean aortic pressure (Pa, mm Hg), distal coronary occlusive (wedge) pressure (Pw, mm Hg) and central venous pressure (Pv, mm Hg). The index is calculated as CFIp=(Pw-Pv)/(Pa-Pv). The pressure derived fractional flow reserve (FFR) and the index of microcirculatory resistance (IMR) are assessed as secondary invasive endpoints to investigate the effect of ECP on the myocardial vasculature. The non-invasive secondary endpoints include symptoms (CCS and NYHA classification), treadmill-testing and analysis of shear-stress related soluble proteins. Conclusions The Art.Net.-2 Trial will report within the next months whether direct evidence can be brought that ECP promotes coronary collateral growth in patients with stable angina pectoris.

Aims Enhanced external counterpulsation (EECP) is a non-invasive and non-pharmacological therapy for patients with symptomatic coronary artery disease (CAD). There are, however, insufficient data to support
the effectiveness of EECP in improving the myocardial mechanical properties of patients with refractory stable angina. We aimed to assess the effects of EECP on myocardial mechanical properties and cardiac functions in CAD patients not eligible for surgical or percutaneous revascularization procedures. Methods and results Twenty patients in New York Heart Association (NYHA) functional Class III and IV angina were evaluated. The mean age of the patients was 63±9 years, and 65% were male. A comprehensive echocardiographic study including an evaluation of the tissue Doppler-based parameters of systolic and diastolic functions was performed before and after the termination of the protocol. EECP was carried out 1 h per day, 5 days per week, for 7 weeks. EECP resulted in a significant increase in peak late diastolic transmitral inflow velocity (0.75±0.14 vs. 0.83±0.20 m/s, p<0.05), propagation velocity (42.35±6.25 vs. 46.00±5.68 cm/s, p<0.05), peak early diastolic velocity of mitral annulus (5.351.79 vs. 5.95±1.10 cm/s, p<0.05), peak systolic velocity (2.51±0.28 vs. 2.67±0.26, p<0.05), and early diastolic velocity (3.24±0.18 vs. 3.52±0.26 cm/s, p<0.01) of all middle segments, peak late diastolic velocity of all basal (4.48±0.58 vs. 4.75±0.70 cm/s, p<0.05) and middle segments (2.82±0.66 vs. 3.25±0.46 cm/s, p<0.01), peak systolic strain rate of all basal (0.76±0.07 vs. 0.99±0.08 1/s, p<0.001) and middle segments (0.75±0.09 vs. 0.94±0.09 1/s, p<0.001), peak systolic strain of basal (11.64±1.51 vs. 13.97±1.52%, p<0.01) and middle segments (11.81±1.15 vs.13.73±1.57%, p<0.001), and left ventricular (LV) ejection fraction (40.25±12.72 vs. 46.25±12.97%, p<0.001). There was also a significant decrease in the ratios of transmitral E/A (0.92±0.41 vs. 1.08±0.46, p<0.05) and E/Ea (12.61±4.22 vs. 15.44±6.96, p<0.05) after EECP therapy. A significant reduction in NYHA angina class (≥1 angina class) was seen in the patients, who completed treatment. Conclusion EECP therapy seemed to improve both regional and global LV systolic and diastolic functions in patients with chronic angina pectoris.


Background Enhanced external counterpulsation (EECP) improves ischemia in patients with refractory angina pectoris, but the mechanism remains unclear. To explore the mechanisms of EECP action, we detected progenitor cells presenting any of the following markers CD34+, CD29+, and CD106+. Methods Growth cytokines-mediated progenitor cell mobilization and associated angiogenesis potential were assessed in a porcine model of hypercholesterolemia. Twenty-four male domestic swines were randomly assigned to 4 groups: normal diet (control, n=6), hypercholesterolemic diet (CHOL, n=6), hypercholesterolemic diet with administration of recombinant human granulocyte colony-stimulating factor (rhG-CSF) (rhG-CSF, n=6), and hypercholesterolemic diet with EECP treatment (EECP, n=6). EECP was applied 2 hours every other day for a total of 36 hours. Serum levels of vascular endothelial growth factor (VEGF) and granulocyte colony-stimulating factor (G-CSF), peripheral blood progenitor cell counts, level of regional angiogenesis, and expression of VEGF and stromal cell derived factor 1α (SDF-1α) in porcine myocardium were assessed, respectively. Results A porcine model of hypercholesterolemia-induced arteriosclerosis was successfully established. There was no significant difference in serum levels of VEGF among the four groups. The serum levels of G-CSF in the EECP group increased significantly at week 15 and week 18 ((38.3±5.6) pg/ml at week 15 vs (26.2±3.7) pg/ml at week 12, P <0.05, and (46.9±6.1) pg/ml at week 18 vs (26.2±3.7) pg/ml at week 12, P <0.01). The serum levels of G-CSF in group 3 increased also significantly after receiving rhG-CSF injection for five days ((150±13.9) pg/ml at week 18 vs (24.8±5.4) pg/ml at week 12, P <0.01). Compared to other groups and other time points, progenitor cell counts increased significantly after 2-hour EECP treatment (108±13 vs 26±6 per 105 leukocytes, P <0.01), but not at week 18. The progenitor cell counts also increased significantly after subcutaneous injection of rhG-CSF for five days compared to the week 12 (baseline) (180±21 vs 25±7 per 105 leukocytes, P <0.01). There was no significant difference among the four groups at other time points. Moreover, the expression of VEGF and SDF-1α and the level of regional angiogenesis in myocardium increased significantly in both EECP and rhG-CSF groups. Conclusions The results demonstrated that EECP could facilitate angiogenesis in the myocardium of atherosclerotic swine by increasing endogenous G-CSF, inducing an enhanced mobilization of progenitor cells and augmenting myocardial expression of VEGF and SDF-1α.
Intervention is increasing both in the management of acute coronary syndromes and chronic stable angina and so too is the need for repeated intervention, where the complexity and procedural risk may be increased as well as the psychological and traumatic burden to patients of increasing age and morbidity. Enhanced external counter pulsation (EECP) is an alternative means of managing coronary disease. This therapy provides augmentation of diastolic flow, through sequential inflation and after-load reduction by simultaneous deflation, from a series of three cuffs applied to calves, lower thigh, upper thigh and buttocks. Currently, EECP is used predominantly in patients with severe angina, who are at high risk and are not suitable for revascularization. It provides a therapeutic and supportive approach to managing such patients regardless of age and comorbidity including those with stable heart failure. Treatment is carried out daily on an outpatient basis for a total of 35 hours over three to seven weeks. RCTs have reported improved symptoms and exercise time to onset of ischaemia. Improved quality of life scores have been reported two years after treatment. EECP provides not only a safe, well tolerated and therapeutic treatment for these patients, but also facilitates a supportive approach through 35 hours of therapy. It improves fitness through passive lower body exercise and often an improvement in well being which may relate to an effect of therapy delivered to the entire circulation. Other benefits include the potential to reduce erectile dysfunction, which is so prevalent and disabling in patients with vascular disease. There are relatively few absolute contraindications. These include, hemodynamically significant aortic valve regurgitation, abdominal aortic aneurysm requiring intervention, and recent history of venous thromboembolism, severe pulmonary hypertension, poorly controlled systolic hypertension and major bleeding diathesis. Provision of EECP should be considered as part of a dedicated service for patients with refractory angina. This service should ideally offer a careful diagnostic assessment and a multidisciplinary approach, including psychological support and rehabilitation and in those with a continuing burden of symptoms the freedom to choose between a psychological approach with CBT, a therapeutic approach with EECP and palliative treatments that can be offered by pain specialists. Growing experimental evidence suggests that EECP may exert its clinical benefits via the effects of shear stress on endothelial function. Combined with optimal medical therapy EECP has been shown to reduce mortality and MI rates and provide a protective effect over five years.

In a prospective study, enhanced external counterpulsation (EECP) was performed for 1 hour each day for 35 days in 47 patients, mean age 61 6 8 years, with prior coronary revascularization who had chronic refractory angina pectoris despite antianginal drugs and who were not candidates for further coronary revascularization. Compared with baseline values, EECP significantly improved anginal symptoms, dyspnea on exertion, and quality of life after 35 days of treatment (p< 0.001) and at 1-year follow up (p<0.001). Compared with the baseline value of 653 ± 249 feet, EECP significantly improved the 6-minute walking distance to 1025 ± 234 feet after 35 days of treatment (p<0.001) and to 1040 ± 221 feet at 1-year follow up (p<0.001). However, EECP did not significantly affect left ventricular ejection fraction, left ventricular end-diastolic and end-systolic volumes, E/A ratio, isovolumic relaxation time, and deceleration time measured by two-dimensional and Doppler echocardiography.


Enhanced external counterpulsation (EECP) is a noninvasive technique that provides beneficial effects for patients with chronic, symptomatic angina pectoris. However, the direct left ventricular effects of EECP have not been studied invasively. We examined invasive right atrial pressure and left ventricular hemodynamics during EECP. Ten patients referred for diagnostic evaluation underwent left heart catheterization from the radial artery. At baseline and during EECP, left ventricular pressure and volume were measured using a micromanometer pressure-conductance catheter, along with recording of right atrial and central aortic pressures. Hemodynamics was recorded at different lower extremity cuff configuration and cuff inflation pressures. As cuff inflation pressure increased, EECP resulted in a dose-dependent increase in right atrial and aortic diastolic pressure (P < 0.0001). The increase in ventricular preload resulted in increased left ventricular volume. Maximum positive (P = 0.0003) and negative left ventricular dP/dt (P < 0.0001) increased. Left ventricular diastolic pressure decreased. There was a neutral effect on myocardial mechanical efficiency. In conclusion, EECP acutely increased right atrial and central aortic diastolic pressure. The increase in preload attenuated the reduction in left ventricular diastolic pressure resulting from systolic unloading. The increased preload counterbalanced the afterload reduction, resulting in a neutral effect on myocardial efficiency.


Refractory angina pectoris, defined as angina refractory to maximal medical therapy and standard coronary revascularization procedures, remains a significant health problem in the United States and the world. Despite a panoply of recent therapeutic advances, patients with refractory angina pectoris are not adequately treated; therefore, scientists have been investigating new technologies to help these patients. The technique of counterpulsation, studied for almost half a century, is considered a safe, highly beneficial, low-cost, noninvasive treatment for these angina patients and now also for those with heart failure. Recent evidence suggests that enhanced external counterpulsation (EECP) therapy may improve symptoms and decrease long-term morbidity via several mechanisms, including improvement in endothelial function, promotion of collateralization, enhancement of ventricular function, improvement in oxygen consumption (VO2), regression of atherosclerosis, and peripheral “training effects” similar to exercise. Numerous clinical trials in the past two decades have shown EECP therapy to be safe and effective for patients with refractory angina, with a clinical response rate averaging 70% to 80%, which is sustained up to 5 years. This review summarizes the current evidence to support EECP’s use in treating refractory angina pectoris.

2008


BACKGROUND Enhanced external counterpulsation (EECP) is a non-invasive treatment option for patients with refractory angina pectoris ineligible to further traditional treatment. The aim of this study was to evaluate the effect of EECP on patients at a Scandinavian medical center and to investigate if outcome can be predicted by analyzing baseline factors. METHODS 86 consecutive patients (70 male, 16 female) were treated with EECP and followed for two years post treatment. Canadian cardiovascular society (CCS) class was analyzed, and medication and adverse clinical events were researched prior to EECP, at the end of the treatment, and at six, 12 and 24 months thereafter. Patients responding to therapy by improving at least one CCS class were compared with those who failed to respond. Any differences in background factors were recorded and analyzed. RESULTS 79% of the patients responded to therapy by
improving at least one CCS class. In general, the CCS class improved by one class after EECP treatment (3.05 before versus 2.14 after treatment). A total of 61.5% of the initial responders showed sustained improvement at the 12-month follow-up while 29% presented sustained improvement after 24 months. Treatment was most effective among patients suffering from CCS class III-IV angina pectoris, while patients suffering from CCS class II angina pectoris improved transiently but failed to show sustained improvement after the 12-month follow-up. Diabetes mellitus and calcium channel antagonists were more common among the non-responders (p < 0.05).

CONCLUSION This study confirms the safety and efficiency of EECP as a treatment option for patients suffering from refractory angina pectoris. The therapy is most beneficial in patients suffering from severe angina (CCS III-IV) while sustained response to therapy could not be verified among patients suffering from CCS class II angina pectoris.


Background Enhanced external counterpulsation (EECP) is a noninvasive treatment of patients with refractory angina. The immediate hemodynamic effects of EECP are similar to intra-aortic balloon pump counterpulsation, but EECP effects on standard blood pressure measurements during and after treatment are unknown. Methods We evaluated systolic blood pressure (SBP) and diastolic blood pressure (DBP) for 108 consecutive patients undergoing EECP. Baseline SBP, DBP, and heart rate were compared for each patient before and after each EECP session, at the end of the course of EECP, and 6 weeks after the final EECP session. Results One hundred eight patients (mean age 66.4 ± 11.2 years, 81% male) completed 36.5 ± 5.1 EECP sessions per patient. Overall, based on 3,586 individual readings, EECP resulted in a decrease in mean SBP of 1.1 ± 15.3 mm Hg at the end of each EECP session (p<0.001), 6.4 ± 18.2 mm Hg at the end the course of EECP (p<0.001), and 3.7 ± 17.8 mm Hg 6 weeks after the final EECP session (p=0.07), with no significant change in DBP or heart rate. Stratifying by baseline SBP, a differential response was demonstrated: SBP increased in the 2 lowest strata (<100 mm Hg and 101-110 mm Hg) and decreased in the remaining strata (p<0.001). Stratified differences were sustained after individual EECP sessions, at the end of the course of EECP, and 6 weeks after the final EECP session and were independent of changes in cardiovascular medications. Conclusions Enhanced external counterpulsation improved SBP in patients with refractory angina. On average, EECP decreased SBP during treatment and follow-up; but for patients with low baseline SBP (<110 mm Hg), EECP increased SBP. The improvements in SBP may contribute to the clinical benefit of EECP.


Introduction As more patients survive coronary events, the prevalence of patients with refractory angina pectoris is increasing. The aim was to evaluate the effects of enhanced external counterpulsation (EECP) and spinal cord stimulation (SCS) and compare with optimal medically treated patients with refractory angina. Methods 153 patients with refractory angina were treated with either EECP, SCS, or were retained on their pharmacological treatment (control). Glyceryl trinitrate usage and Canadian Cardiovascular Society classification were registered at baseline, 6 and 12 months after therapy. Results Both EECP and SCS reduced the angina as compared with controls (p< 0.001). Patients treated with EECP showed a more effective reduction as compared with SCS patients (p< 0.05). Both treatments resulted in significantly decreased glyceryl trinitrate usage at 6 and 12 months follow-up (p< 0.001). The nitrate consumed was unaltered in the controls. Discussion The results from this study show that both EECP and SCS therapy reduce angina in patients with refractory angina pectoris; the response to EECP was slightly more effective than that to SCS. Thus, EECP can be used as an alternative treatment for patients not responding to electrical stimulation. The beneficial effects in the treated groups were maintained during the 12 months follow-up period.
Background The adverse effects of tobacco abuse on cardiovascular outcomes are well-known. However, the impact of passive smoke exposure on angina status and therapeutic response is less well-established. We examined the impact of second-hand smoke (SHS) exposure on symptomatic improvement in patients with chronic ischemic coronary disease undergoing enhanced external counterpulsation (EECP). Methods This observational study included 1,026 non-smokers (108 exposed and 918 not-exposed to SHS) from the Second International EECP Patient Registry. We also assessed angina response in 363 current smokers. Patient demographics, symptomatic improvement and quality of life assessment were determined by self-report prior and after EECP treatment. Results Non-smoking SHS subjects had a lower prevalence of prior revascularization (85% vs 90%), and had an increased prevalence of stroke (13% vs 7%) and prior smoking (72% vs 61%; all \( p < 0.05 \)) compared to non-smokers without SHS exposure. Despite comparable degrees of coronary disease, baseline angina class, medical regimens and side effects during EECP, fewer SHS non-smokers completed a full 35-hour treatment course (77% vs 85%, \( p = 0.020 \)) compared to non-smokers without SHS. Compared to non-smokers without SHS, non-smoking SHS subjects had less angina relief after EECP (angina class decreased ≥ 1 class: 68% vs 79%; \( p = 0.0082 \)), both higher than that achieved in current smokers (66%). By multivariable logistic regression, SHS exposure was an independent predictor of failure to symptomatic improvement after EECP among non-smokers (OR 1.81, 95% confidence intervals 1.16–2.83). Conclusion Non-smokers with SHS exposure had an attenuated improvement in anginal symptoms compared to those without SHS following EECP.


Background Enhanced external counterpulsation (EECP) is a noninvasive, pneumatic technique that provides favourable effects in patients with coronary artery disease. The objective of this study was to describe the long-term effect of EECP on endothelial function in patients with ischaemic cardiomyopathy. Method The study was performed in 15 patients with ischaemic cardiomyopathy. All subjects were treated with EECP 1-h per day, 5 days a week, over 7 weeks (totally 35 h). Endothelium-dependent and -independent relaxation was assessed by flow-mediated dilation (FMD) and nitroglycerine-mediated dilatation (NMD). In each patient, FMD and NMD measurements were performed before, at midcourse (day 17th) and after completion of EECP course (day 35th). In addition, FMD index was assessed 1 month after completion of EECP therapy. Results Results showed that EECP was associated with a significant improvement in FMD index after 35 hours of EECP (10.95±4.1% vs. 7.40±4.9% for baseline, \( p < 0.05 \)). NMD index didn’t significantly alter during the EECP therapy. Also, 1 month after completion of EECP, FMD index returned to baseline (7.51±4.4% vs. 7.40±4.9%, respectively, \( p < 0.05 \)). EECP acutely improved endothelial function in ischaemic cardiomyopathic patients. However, after 1-month completion of treatment, endothelium-dependent vasorelaxation returned to baseline. Conclusion It seems that improvement of endothelial function is not the main mechanism of long-term EECP treatment and other mechanisms should be considered.


BACKGROUND The management of patients who suffer from medically refractory angina and are unsuitable for conventional revascularization therapy is often unsatisfactory. Enhanced external counterpulsation (EECP) is a noninvasive treatment that is safe and effective immediately after a course
of treatment. However, the duration of benefit is less certain. HYPOTHESIS To evaluate the 3-year outcome of EECP treatment. METHODS One thousand four hundred and twenty seven patients from 36 centers registered in the International EECP Patient Registry (IEPR)-Phase 1 was prospectively followed for a median of 37 months. Two hundred and twenty patients (15.4%) died, while 1,061 patients (74.4%) completed their follow-up. RESULTS The mean age was 66 +/- 11 years and 72% were men. Seventy-six percent had multivessel coronary disease for 11 +/- 8 years. Eighty-eight percent had a prior percutaneous or surgical revascularization and 82% were unsuitable for further coronary intervention. Immediately post-EECP, the proportion of patients with severe angina (Canadian Cardiovascular Angina Classification [CCS] III/IV) were reduced from 89% to 25%, < 0.001. The CCS class was improved by at least 1 class in 78% of the patients and by at least 2 classes in 38%. This was sustained in 74% of the patients during follow-up. Thirty-six percent of the patients had CCS II or less angina, which was better than pre-EECP state without a major adverse cardiovascular event during follow-up. More severe baseline angina and a history of heart failure or diabetes were independent predictors of unfavorable outcome. CONCLUSION An EECP improves angina and quality of life immediately after a course of treatment. For most of the patients, these beneficial effects are sustained for 3 years.


Digital imaging and communications in medicine (DICOM) Standard has a detailed description on the Information Object Definition (IOD) of all kinds of medical images and waveforms. With the development and application of DICOM, all medical imaging and waveform devices will support the standard. This article describes the method and implementation on how to encapsulate the EECP Hemodynamic Waveforms data acquired from EECP device, integrating patient information, EECP physiological parameters, and diagnosis and treat information into DICOM Hemodynamic Waveform file. We define Private Data Elements to encode and represent EECP parameters which haven’t been registered as Standard Data Elements. This is the semantic extension of DICOM applied in EECP. The paper introduces following parts in detail: the structure of DICOM waveform file, Data Element, Nesting of Data Sets, the Waveform IOD Modules and the specification of Private Data Element. Then the method and process of our program are analyzed in depth. According to object-oriented methodology, firstly, Data Element, Nesting of Data Sets and waveform IOD with their corresponding operations and services are respectively abstracted into classes. Then the waveforms data and other attributes are assigned to the corresponding Data Members of the waveform class. Finally, they are stored into a DICOM waveform file by invoking related functions.


OBJECTIVES External counter pulsation therapy (ECPT) offers symptomatic relief and improves ischemia in patients with refractory angina pectoris. We aimed to determine the effects of ECPT on circulating endothelial progenitor cells (EPCs). METHODS We prospectively studied 25 patients with angina pectoris treated with ECPT (n = 15) or receiving standard care (n = 10). The number of EPCs positive for CD34 and kinase insert receptor domain receptor (KDR) was determined by flow cytometry and the number of colony-forming units (CFUs) was assessed in a 7-day culture, before ECPT and after 9 weeks. RESULTS ECPT improved anginal score from a median of 3.0 to 2.0 (< 0.001). Concomitantly, ECPT increased EPC number from a median of 10.2 to 17.8/10(5) mononuclear cells (p < 0.05), and CFUs from 3.5 to 11.0 (p = 0.01). Flow-mediated dilatation was improved by ECPT from 7.4 to 12.2% (< 0.001) and correlated with EPC-CFUs (r = 0.461, p = 0.027). The levels of asymmetric dimethylarginine were reduced by ECPT from 0.70 to 0.60 micromol/l (< 0.01). In contrast, the same parameters did not change in the control group, before and after follow-up. CONCLUSIONS The present pilot study shows, for the first time, that ECPT is associated with increased number and colony-forming capacity of circulating EPCs.
Cardiovascular disease is associated with chronic low-level inflammation, as evidenced by elevated circulating proinflammatory cytokines. Experimental evidence suggests that inflammation can be suppressed under conditions of high shear stress. This study was conducted to examine the effects of enhanced external counterpulsation (EECP), a noninvasive therapy that increases endothelial shear stress, on circulating levels of inflammatory biomarkers and adhesion molecules in patients with angina pectoris. Twenty-one patients were randomly assigned to either 35 1-hour treatments at cuff pressures of 300 mm Hg (EECP; n=12) or 75 mm Hg (sham; n=9). Plasma tumor necrosis factor-alpha, monocyte chemoattractant protein-1, and soluble vascular cell adhesion molecule-1 were measured before and after 35 1-hour sessions of treatment or sham. Patients in the EECP group demonstrated reductions in tumor necrosis factor-alpha (6.9+/−2.7 vs 4.9+/−2.5 pg/ml, p<0.01; −29%) and monocyte chemoattractant protein-1 (254.9+/−55.9 vs 190.4+/−47.6 pg/ml, p<0.01; −19%) after treatment, whereas there was no change in the sham group. Changes in soluble vascular cell adhesion molecule-1 were not observed in either group. In conclusion, 35 sessions of EECP decreased circulating levels of proinflammatory biomarkers in patients with symptomatic coronary artery disease.

2007


**PURPOSE** To evaluate whether enhanced external counterpulsation (EECP) exerts an effect on myocardial perfusion. **METHODS** Eleven patients with angina were studied before and after 35 sessions of EECP treatment. Myocardial perfusion was quantified with positron emission tomography and intravenous 13N-ammonia at rest and after dipyridamole, by means of a two-compartment mathematical model. **CONCLUSION** The results suggest that EECP has no effect on myocardial perfusion. However, because of the small number of patients in this study and highly variable clinical responses, additional studies are required to corroborate this finding. The beneficial effects of EECP appear to be mediated by other mechanisms.


This study assessed the effects of a course of enhanced external counterpulsation (EECP) therapy on systolic and diastolic cardiac function using echocardiography to measure left ventricular ejection fraction (LVEF), end-systolic volume (ESV), end-diastolic volume (EDV), systolic wave (Sm), early diastolic wave (Ea), Vp, E/Ea, E/Vp, and diastolic function grade in 25 patients before and after 35 hours of EECP. EECP reduced ESV and EDV and increased ejection fraction significantly in patients with baseline LVEF ≤50% (p=0.018, 0.013, 0.002), baseline E/Ea ≥14 (P=.032, .038, .007), baseline grade II or III diastolic dysfunction (decreased compliance) (P=.014, .032, .027), baseline Ea <7 cm/s (P=.015, .024, .001), and baseline Sm <7 cm/s (P=.017, .016, .006), but not in patients with baseline LVEF >50%, baseline E/Ea <14, baseline normal diastolic function or grade I diastolic dysfunction (impaired relaxation), baseline Ea ≥7 cm/s, and Sm ≥7 cm/s. These results demonstrate improved systolic and diastolic function in selected patients and provide new insight into potential clinical applications of EECP.

Between 25,000 and 75,000 new cases of angina refractory to maximal medical therapy and standard coronary revascularization procedures are diagnosed each year. In addition, heart failure also places an enormous burden on the U.S. health care system, with an estimated economic impact ranging from $20 billion to more than $50 billion per year. The technique of counterpulsation, studied for almost one-half century now, is considered a safe, highly beneficial, low-cost, noninvasive treatment for these angina patients, and now for heart failure patients as well. Recent evidence suggests that enhanced external counterpulsation (EECP) therapy may improve symptoms and decrease long-term morbidity via more than 1 mechanism, including improvement in endothelial function, promotion of collateralization, enhancement of ventricular function, improvement in oxygen consumption (VO_2), regression of atherosclerosis, and peripheral training effects similar to exercise. Numerous clinical trials in the last 2 decades have shown EECP therapy to be safe and effective for patients with refractory angina with a clinical response rate averaging 70% to 80%, which is sustained up to 5 years. It is not only safe in patients with coexisting heart failure, but also is shown to improve quality of life and exercise capacity and to improve left ventricular function long-term. Interestingly, EECP therapy has been studied for various potential uses other than heart disease, such as restless leg syndrome, sudden deafness, hepatorenal syndrome, erectile dysfunction, and so on. This review summarizes the current evidence for its use in stable angina and heart failure and its future directions.

- **Sajja V, Dod H, Beto R, Jain AC, Hobbs GR, Finkel MS. An Analysis of the Efficacy and Safety of Enhanced External Counterpulsation at West Virginia University Hospitals. The West Virginia Medical Journal. 2007 May-Jun;103(3):10-12.**

A retrospective analysis was conducted of 79 consecutive patients who underwent enhanced external counterpulsation (EECP) at West Virginia University Hospitals during the period of November 1998 to September 2005 to determine its efficacy and safety in treating angina. A chart review and/or phone survey was performed to analyze pertinent clinical data (sublingual nitroglycerin use and angina class) pre and post EECP. A total of 60 (76%) patients who were referred for EECP successfully finished the 35 treatments. Seventy-five percent of the patient population improved at least one angina class after a full course of treatment. Therapy was discontinued due to adverse effects in 12 (15%) patients. Statistically significant improvements in angina class and reduction in anti-angina medications were observed in every co-morbid subgroup analyzed, including patients with peripheral vascular disease, diabetes, hyperlipidemia, hypertension, smoking, Post-MI, and LVEF < 40% (p<0.05, Wilcoxon Signed-Rank test). Overall, EECP was effective in improving angina as reflected in a substantial reduction in antiangina medications in 59 (75%) patients.


OBJECTIVE We evaluated the degree of residual angina on the outcomes of enhanced external counterpulsation (EECP) therapy for chronic stable angina. BACKGROUND Angina refractory to medical therapy is common in the pool of patients who are not completely revascularized by angioplasty or bypass surgery. METHODS We examined 902 patients enrolled from 1998 to 2001 in the Second International Enhanced External Counterpulsation Patient Registry. Baseline and outcome variables were stratified by the last recorded Canadian Cardiovascular Society class. RESULTS Residual Class 3 (12.1%) or 4 (2.3%) angina was uncommon among patients with severe coronary artery disease after treatment with EECP. Prevalence of diabetes, hypertension, dyslipidemia, and heart failure was similar among the anginal post-EECP anginal classes. Multivessel coronary disease was more common in those with higher-grade angina at completion. More frequent and severe angina at entry was more common in those with the higher anginal classes at EECP (p<0.001). There were no differences in the rates of chronic medications utilized or prior revascularization. At 3-year follow-up, rates of death, myocardial infarction, percutaneous coronary intervention, and coronary artery bypass surgery tended to be higher across increasing residual angina classes. The composite cardiac event rates were 34%, 33%, and 44% for those with Class 0, Class 1/2, and Class 3/4 angina at EECP completion (p=0.01), respectively. Multivariate analysis for the composite endpoint found residual Class 3/4 angina (OR=1.59, 95% CI=1.19-
2.17, p=0.002), diabetes (OR=1.57, 95% CI=1.23-2.01, p=0.0003), age (per decile OR=1.17, 95% CI=1.04-1.31, p=0.007), and greater EECP augmentation (OR=0.79, 95% CI=0.65-0.96, p=0.02) as significant predictors. CONCLUSIONS Residual high-grade angina after EECP occurs in those with more severe angina and multivessel disease at baseline and is associated with cardiac events over the next 3 years. These data suggest that close clinical observation and intensive management of those with high-grade angina post-EECP are warranted.


Background Enhanced external counterpulsation (EECP) is a noninvasive method previously shown to improve measures of myocardial ischemia in patients with coronary artery disease. However, the concomitant effects of EECP on large and small arterial properties have been poorly examined. In a randomized controlled study, we investigated whether arterial stiffness and resistance of the carotid circulation are altered by EECP. Methods Thirty patients with angiographically demonstrated coronary artery disease were randomized into two groups to receive either ‘sham’ or ‘active’ EECP therapy for 35 1-hour sessions. The β stiffness index was calculated by the ln(Ps/Pd)/DD equation where Ps and Pd = systolic and diastolic blood pressure, and DD = the ratio between carotid pulse and diastolic diameter, measured by ultrasound sequential frames during the cardiac cycle. Carotid vascular resistance was calculated as the ratio between mean arterial pressure and mean common carotid blood flow. Results No significant between-group differences were seen in clinical characteristics or carotid hemodynamics at baseline. The β stiffness index and carotid vascular resistance were significantly reduced after 35 h of active EECP (p<0.01), and the decrease was significantly different when compared with controls (p<0.05 for β stiffness index and p<0.001 for carotid vascular resistance). These reductions persisted after multiple covariate adjustment. Conclusions This study suggests that EECP exerts clear arterial effects on large and small vessels of the carotid circulation. The combined effects on arterial stiffness and vascular resistance are of particular interest in cardiovascular disease involving reduction in blood flow, in which techniques that increase regional blood flow may be beneficial.


BACKGROUND Enhanced external counterpulsation (EECP) is a circulation assist device that may improve endothelial dysfunction by increasing shear stress. Chronic exposure of vascular endothelial cells and vascular smooth muscle cells to relatively high physiological shear stress has antiproliferative and vasoprotective effects. The present study hypothesizes that EECP inhibits intimal hyperplasia and atherogenesis by modifying shear stress-responsive gene expression. METHODS AND RESULTS Thirty-five male pigs were randomly assigned to 3 groups: high-cholesterol diet (n=11), high-cholesterol diet plus EECP (n=17), and usual diet (control; n=7). The coronary arteries and aortas were collected for histopathological study and immunohistochemical and Western blot analysis. The peak diastolic arterial wall shear stress during EECP increased significantly compared with before EECP (49.62+/−7.28 dyne/cm2; p=0.001). Intimal hyperplasia was observed in the coronary arteries of the high-cholesterol diet group, whereas in animals receiving EECP, the intima-to-media area ratio was significantly decreased by 41.59% (21.27+/−10.00% versus 36.41+/−16.69%; p=0.008). Hypercholesterolemia attenuated the protein expression of endothelial NO synthase and enhanced the phosphorylation of extracellular signal-regulated kinases 1/2. EECP treatment alleviated these adverse changes. CONCLUSIONS EECP reduces hypercholesterolemia-induced endothelial damage, arrests vascular smooth muscle cell proliferation and migration, decreases proliferating cell nuclear antigen proliferative index, suppresses extracellular matrix formation, and eventually inhibits intimal hyperplasia and the development of atherosclerosis by increasing the arterial wall shear stress, which in turn activates the endothelial NO synthase/NO pathway and probably suppresses extracellular signal-regulated kinases 1/2 overactivation.

BACKGROUND Enhanced external counterpulsation (EECP) is a novel, potentially beneficial adjunct therapy used for angina pectoris. We assessed the efficacy of this method in relieving angina and improving objective measures of myocardial ischaemia. METHODS All patients (67) who referred for EECP to Shahid Chamran Hospital, Isfahan, Iran from 2002 to 2005 were included. Demographic data, coronary artery disease (CAD) risk factors and baseline angiographic data were collected. Anginal symptoms, Canadian Cardiovascular Society (CCS) functional class, echocardiographic parameters (ejection fraction, left ventricular end-diastolic and end-systolic diameters) and exercise test duration before and after the treatment was compared. RESULTS Seventy-seven per cent of patients who had undergone EECP had a positive clinical response. Exercise test duration and CCS functional class improved after the treatment. However, EECP had no significant effect on echocardiographic parameters. Efficacy was independent of age, gender, CAD risk factors, prior CCS functional class and echocardiographic parameters. Patients without left main artery involvement and those who had at least one non-obstructed artery demonstrated a greater likelihood of improvement. CONCLUSION The results of this study suggested that EECP is a safe, well tolerated, and significantly effective treatment for angina pectoris.


BACKGROUND AND PURPOSE We hypothesized that symptom improvement from enhanced external counterpulsation (EECP) is related to improved heart rate variability (HRV). METHODS This prospective, multicenter study enrolled 27 patients with angina who underwent 48-hour ambulatory electrocardiogram monitoring at baseline, immediately after 35 hours of EECP, and at 1 month. Primary end points included change in time-domain (SD of normal-to-normal intervals) and frequency-domain HRV. RESULTS Twenty-four patients completed the full course of EECP therapy and 3 ambulatory electrocardiograms. There were no significant changes in time-domain HRV measures after EECP. Patients younger than 65 years and those with heart failure had improved SD of normal-to-normal interval after EECP (p=0.02). Although frequency-domain HRV measures did not change in the overall cohort, patients with diabetes had improved daytime low-frequency power (p=0.016). CONCLUSIONS There was no significant change in the time- or frequency-domain HRV measures after EECP. In diabetic individuals, there was an increase in low-frequency HRV, which has been associated with reduced mortality.


Enhanced external counterpulsation (EECP) is a noninvasive counterpulsation technique that reduces angina and improves exercise capacity in patients with coronary artery disease. Diastolic coronary perfusion is augmented by pneumatic compression of 3 sets of cuffs wrapped around the lower extremities. Although central hemodynamic changes are well investigated, almost no data exist about the changes of peripheral circulation during EECP. In this study, 12 patients with angina and angiographic evidence of coronary artery disease were treated for 1 hour with EECP. In these patients, peripheral artery disease was excluded by duplex sonography. The patients rested 1 hour before EECP in supine position, and they remained in that position for 1 hour after the procedure. Changes of flow volumes and flow pattern of the posterior tibial artery and the brachial artery were measured by sonography at the end of all 3 periods. Furthermore, we measured the concentration of circulating prostanoids at these 3 time points. Averaged flow volume of the posterior tibial artery decreased to 69% ± 23% (p<0.05) during EECP and increased to 133% ± 34% (p<0.05) of baseline 1 hour after the procedure. In contrast, the averaged flow volume of the brachial artery increased by 9% ± 4% (p<0.05) during EECP and returned to baseline values after EECP. The flow pattern of the posterior tibial artery showed a second early diastolic antegrad flow caused by the cuff inflation and a reverse end-diastolic flow after the deflation of the cuffs. These flow changes caused an increase of the pulsatility index by Gosling (397% during EECP), returning...
Patients with refractory angina often suffer from erectile dysfunction. Enhanced external counterpulsation (EECP) decreases symptoms of angina, and increases nitric oxide release. This study evaluated the effect of EECP on sexual function in men with severe angina. The International Index of Erectile Function (IIEF) was used to assess erectile function of severe angina patients enrolled in the International EECP Patient Registry. Their symptom status, medication use, adverse clinical events and quality of life were also recorded before and after completing a course of EECP. A cohort of 120 men (mean age 65.0 ± 9.7) was enrolled. The men had severe coronary disease with 69% having a prior myocardial infarction, 90% prior coronary artery bypass graft or percutaneous coronary intervention, 49% with three vessel coronary artery disease, 86% were not candidates for further revascularisation, 71% hypertensive, 83% dyslipidaemia, 42% diabetes mellitus, 75% smoking and 68% using nitrates. Functional status was low with a mean Duke Activity Status Inventory score of 16.6 ± 14.8. After 35 h of EECP anginal status improved in 89%, and functional status in 63%. A comparison of the IIEF scores pre and post-EECP therapy demonstrated a significant improvement in erectile function from 10.0 ± 1.0 to 11.8 ± 1.0 (p = 0.003), intercourse satisfaction (4.2 ± 0.5 to 5.0 ± 0.5, p = 0.009) and overall satisfaction (4.7 ± 0.3 to 5.3 ± 0.3, p = 0.001). However, there were no significant changes in orgasmic function (4.2 ± 0.4 to 4.6 ± 0.4, p = 0.19) or sexual desire (5.3 ± 0.2 to 5.5 ± 0.2). The findings suggest that EECP therapy is associated with improvement in erectile function in men with refractory angina.

Background Enhanced external counterpulsation (EECP) currently is used as an outpatient therapy for patients with refractory chronic angina. Hypothesis We sought to determine the safety and feasibility of a portable EECP unit to treat patients with acute coronary syndrome and/or cardiogenic shock in the coronary care unit (CCU). Methods Ten patients with acute coronary syndrome and/or cardiogenic shock who were not considered candidates for invasive intra-aortic balloon counterpulsation (IABP) by the treating cardiologist were prospectively enrolled in this single-center study. Each patient received 2-4 one-hour EECP treatments performed at the bedside in the CCU. Anticoagulation or recent femoral access was not an exclusion criterion. Results The mean age was 58 ± 19 years (range 28-81), and half were women. Patients had either acute coronary syndrome alone (n = 4), cardiogenic shock alone (n = 3), or both (n = 3). The cardiac indications for study enrollment included: acute inferior wall ST-segment elevation myocardial infarction with cardiogenic shock (n = 2), non-ST-segment elevation myocardial infarction with postinfarction angina (n = 2) or heart failure (n = 1), unstable angina with refractory rest angina (n = 2), cardiogenic shock from ischemic cardiomyopathy with severe mitral regurgitation (n = 1), and cardiogenic shock from nonischemic cardiomyopathy (n = 2). No adverse events were recorded during or as a consequence of EECP therapy, including no bleeding complications, no heart failure exacerbations, and no skin breakdown. The portable EECP unit did not interfere with ongoing critical care nursing. Conclusions EECP is safe and feasible for acute bedside therapy of critically ill patients with acute coronary syndrome and/or cardiogenic shock who are not candidates for IABP.

References

Introduction Recently it has been demonstrated that enhanced external counterpulsation (EECP) could improve erectile dysfunction (ED) in patients with refractory ischemic heart disease (IHD).

Aim To assess the effect of risk factors on the efficacy and the satisfaction rate of EECP in patients with coronary artery disease (CAD)-associated ED. Main Outcome Measures To assess the effect of risk factors on EECP efficacy and satisfaction rate, we compared the pre- and post-EECP responses to erectile function domain, Q3, and Q4 in patients with and without risk factors. Overall satisfaction and global efficacy question (GEQ) were also assessed. Methods A total of 44 male consecutive patients with intractable angina caused by coronary insufficiency which cannot be controlled by conventional therapy were enrolled in this study. Patients were screened and followed up for ED using erectile function domain of the International Index for Erectile Function. A thorough sexual, medical, and psychosocial history was taken from all patients. Results All patients had severe diffuse triple vessels disease. They all had class III or IV angina. They were receiving the maximal antianginal pharmacotherapy. The mean age was 57.1 ± 5.6 years. Of the patients, 63.9% were below 60 years, and 86.4% were current or ex-smokers. There were significant differences between pre- and post-EECP regarding erectile function domain, Q3, and Q4. The sociodemographic variables were not significantly different among the studies groups and had not affected the GEQ or overall satisfaction. Overall satisfaction and GEQ were negatively influenced by smoking and presence of more than two risk factors. However, diabetes, hypertension, dyslipidemia, myocardial infraction, and obesity have not had such effects. Conclusions The efficacy and satisfaction rate of EECP in patients with CAD-associated ED were negatively influenced by presence of risk factors; however, the global efficacy and the overall patients' satisfaction were encouraging.


Introduction Enhanced external counterpulsation (EECP) is a noninvasive outpatient treatment used for patients with intractable angina refractory to aggressive surgical and medical treatment. Recent results have demonstrated a positive impact of EECP on patients with ischemic heart disease (IHD)-associated erectile dysfunction (ED). Aim To assess the effect of IHD duration and number of EECP courses on efficacy and satisfaction rate of EECP on patients with IHD-associated ED. Main Outcome Measures We compared pre- and post-EECP responses to erectile function (EF) domain, Q3 and Q4 of the International Index of Erectile Function score in patients who received one or two courses of EECP and those who had <5 or ≥ 5-years duration of IHD. Methods As mentioned in part I a total of 44 male patients with intractable angina caused by coronary insufficiency were enrolled in this study. Treatment course of EECP consists of 35 1-hour sessions over 7 weeks. Another 35 1-hour sessions over another 7 weeks were offered to patients who received one course and required a second course because of no or minimal improvement from class IV to class III angina after the first course. Results Patients who received only one course (N = 34) had significantly higher EF domain, Q3 and Q4, in pre- and post-EECP results than patients who received two courses (N = 10) after they completed the first course. Patients who had <5-years duration of IHD had significantly higher pre- and post EECP than patients who had ≥5 years regarding EF domain, Q3 and Q4. Considering the global efficacy question, overall satisfaction, and angina, there were significant improvements of post EECP in patients with <5 years than in patients with ≥5-years duration of IHD. Conclusion The efficacy and satisfaction rate of EECP in patients with IHD-associated ED were negatively influenced by longer duration of IHD and requirement of a second course of EECP.

- **Soran O, Kennard ED, Bart BA, Kelsey SF. Impact of External Counterpulsation Treatment on Emergency Department Visits and Hospitalizations in Refractory Angina Patients with Left Ventricular Dysfunction. Congestive Heart Failure. 2007 Jan-Feb;13(1):36-40.**

Patients with refractory angina and left ventricular (LV) dysfunction exert an enormous burden on health care resources primarily because of the number of recurrent emergency department (ED) visits and hospitalizations. Enhanced external counterpulsation (EECP) therapy has emerged as a treatment option for patients with angina and LV dysfunction and has been shown to improve clinical outcomes and LV
function. Improvements in symptoms and laboratory assessments in these patients, however, do not necessarily correlate with a reduction in ED visits and hospitalizations. This is the first study to assess the impact of EECP therapy on ED visits and hospitalization rates at 6-month follow-up. This prospective cohort study included 450 patients with LV dysfunction (ejection fraction <or=40%) treated with EECP therapy for refractory angina. Clinical outcomes, number of all-cause ED visits, and hospitalizations within the 6 months before EECP therapy were compared with those at 6-month follow-up. Despite the unfavorable risk profile, refractory angina patients with LV dysfunction achieved a substantial reduction in all-cause ED visits and hospitalization rates at 6-month follow-up. EECP therapy appears to offer an effective adjunctive treatment option for this group of patients.

2006


The Prospective Evaluation of Enhanced External Counterpulsation in Congestive Heart Failure (PEECH) trial demonstrated that enhanced external counterpulsation (EECP) therapy increased exercise duration and improved functional status and quality of life without affecting peak oxygen consumption. The authors present data from a prespecified subgroup of elderly patients (65 years or older) enrolled in the PEECH trial. The 2 co-primary end points were the percentage of subjects with a >60-second increase in exercise duration and the percentage of subjects with a >1.25-mL/kg/min increase in peak volume of oxygen consumption. At 6-month follow-up, the exercise responder rate was significantly higher in EECP patients compared with controls (P=.008). Further, in contrast to the overall PEECH study, the EECP group demonstrated a significantly higher responder rate for peak oxygen consumption (P=.017). The authors conclude that an older subgroup of PEECH subjects confirms the beneficial effect of EECP in patients with chronic, stable, mild-to-moderate heart failure.

- **Lawson WE, Barsness G, Michaels AD, Soran O, Kennard ED, Kelsey SF, Hui JCK. Effectiveness of Repeat Enhanced External Counterpulsation for Refractory Angina in Patients Failing to Complete an Initial Course of Therapy. Cardiology. 2006 Nov 1;108(3):170-175 [Epub ahead of print]**

Aims This study examined the causes and results of retreatment of patients who failed to complete an initial 35-hour Enhanced External Counterpulsation (EECP) course. Methods and Results Data of 2,311 successive angina patients from the International EECP Patient Registry were analyzed; 86.5% completed their EECP course (Complete cohort). Of the 13.5% patients failing to complete the initial course (Incomplete cohort), 28.3% had repeat EECP within 1 year vs. 10.1% of the Complete group. The predictors of failure to complete the initial course of EECP were: female gender, heart failure, use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and use of nitroglycerin. For the Complete group, 83.4% had a reduction of at least one Canadian Cardiovascular Society (CCS) class after their initial EECP course, vs. 21.7% in the Incomplete group (p = 0.001). After repeat treatment, 66.2% of the Incomplete group achieved at least one CCS class reduction vs. 69.4% of the Complete group (p = NS) undergoing retreatment. The independent predictors for those who return to successfully complete their second course were patients who stopped their first course because of clinical events, and candidacy for coronary artery bypass grafting at the time of initial treatment. Conclusion The results of retreatment of those who failed to complete their initial EECP course were comparable to those who completed their initial treatment, with similar reductions of CCS angina class.

Over the past decade, the frequency of use of enhanced external counterpulsation (EECP) has increased in patients with angina, irrespective of medical therapy and coronary revascularization status. Many patients referred for EECP have one or more comorbidities that could affect this treatment's efficacy, safety, or both. By use of data from more than 8,000 patients enrolled in the International EECP Patient Registry, we provide practical guidelines for the selection and treatment of patients. We have focused on considerations for patients who have one or more of the following characteristics: age older than 75 years, diabetes, obesity, heart failure, and peripheral vascular disease. We have also reviewed outcomes and treatment recommendations for individuals with poor diastolic augmentation during treatment, for those with atrial fibrillation or pacemakers, and for those receiving anticoagulation therapy. Lastly, we examined relevant data regarding extended courses of EECP, repeat therapy, or both. While clinical studies have demonstrated the usefulness of EECP in selected patients, these guidelines permit recommendations for the extended application of this important treatment to subsets of patients excluded from clinical trials.

- **Cohn PF. Enhanced External Counterpulsation for the Treatment of Angina Pectoris. Progress in Cardiovascular Diseases. 2006 Sep-Oct;49(2):88-97.**

The treatment of refractory chronic angina pectoris presents an increasing problem for all physicians caring for patients with coronary artery disease because of the large number of individuals who have either failed multiple revascularization procedures or are not appropriate candidates for such procedures. The aim of this study was to review the safety, efficacy, and clinical applicability of a noninvasive technique (external counterpulsation) for the treatment of angina pectoris. A MEDLINE search for all English language abstracts, meeting presentations, journal articles, and reviews from 1960 through December 2005 was conducted. Of the 194 citations in the literature, 60 appeared before 1983 when the enhanced version of the technique (the one that is presently used) was first reported. Criteria for further evaluation of the 134 post-1983 citations were either (1) randomized trial, (2) observational study of at least 10 patients, or (3) investigations into possible mechanisms. Of the 134 citations, 45 were used for data extraction. Observational studies from the United States, Asia, and Europe have demonstrated improvement in symptoms, reduction in anginal episodes, better quality of life, and improved exercise performance in over 5000 patients. The only randomized study (Multicenter Study of Enhanced External Counterpulsation) confirmed these findings as well as the continuation of clinical benefits at least 1 year post-treatment. Although the mechanisms by which diastolic augmentation achieves these beneficial results are still under investigation, this is a promising noninvasive therapy in a group of patients with limited treatment options.


BACKGROUND Enhanced external counterpulsation (EECP) is a noninvasive method previously shown to improve measures of myocardial ischemia in patients with coronary artery disease. However, the concomitant effects of EECP on large and small arterial properties have been poorly examined. In a randomized controlled study, we investigated whether arterial stiffness and resistance of the carotid circulation are altered by EECP. METHODS Thirty patients with angiographically demonstrated coronary artery disease were randomized into two groups to receive either ‘sham’ or active EECP therapy for 35 1-hour sessions. The beta stiffness index was calculated by the \( \ln(P_{s}/P_{d})/DD \) equation where \( P_s \) and \( P_d \) = systolic and diastolic blood pressure, and \( DD = \) the ratio between carotid pulse and diastolic diameter, measured by ultrasound sequential frames during the cardiac cycle. Carotid vascular resistance was calculated as the ratio between mean arterial pressure and mean common carotid blood flow. RESULTS No significant between-group differences were seen in clinical characteristics or carotid hemodynamics at baseline. The beta stiffness index and carotid vascular resistance were significantly reduced after 35 h of active EECP (\( p < 0.01 \)), and the decrease was significantly different when compared with controls (\( p < 0.05 \) for beta stiffness index and \( p < 0.001 \) for carotid vascular resistance). These reductions persisted after multiple covariate adjustment. CONCLUSIONS This study suggests that EECP exerts clear arterial effects on large and small vessels of the carotid circulation. The combined effects on arterial stiffness and
vascular resistance are of particular interest in cardiovascular disease involving reduction in blood flow, in which techniques that increase regional blood flow may be beneficial.


OBJECTIVES The PEECH (Prospective Evaluation of Enhanced External Counterpulsation in Congestive Heart Failure) study assessed the benefits of enhanced external counterpulsation (EECP) in the treatment of patients with mild-to-moderate heart failure (HF). BACKGROUND Enhanced external counterpulsation reduced angina symptoms and extended time to exercise-induced ischemia in patients with coronary artery disease, angina, and normal left ventricular function. A small pilot study and registry analysis suggested benefits in patients with HF. METHODS We randomized 187 subjects with mild-to-moderate symptoms of HF to either EECP and protocol-defined pharmacologic therapy (PT) or PT alone. Two co-primary end points were pre-defined: the percentage of subjects with a 60 s or more increase in exercise duration and the percentage of subjects with at least 1.25 ml/min/kg increase in peak volume of oxygen uptake (VO\textsubscript{2}) at 6 months. RESULTS By the primary intent-to-treat analysis, 35% of subjects in the EECP group and 25% of control subjects increased exercise time by at least 60 s (p = 0.016) at 6 months. However, there was no between-group difference in peak VO\textsubscript{2} changes. New York Heart Association (NYHA) functional class improved in the active treatment group at 1 week (p < 0.01), 3 months (p < 0.02), and 6 months (p < 0.01). The Minnesota Living with Heart Failure score improved significantly 1 week (p < 0.02) and 3 months after treatment (p = 0.01). CONCLUSIONS In this randomized, single-blinded study, EECP improved exercise tolerance, quality of life, and NYHA functional classification without an accompanying increase in peak VO\textsubscript{2}.


OBJECTIVES To determine if arterial properties and wave reflection characteristics are favorably altered after enhanced external counterpulsation (EECP) treatment in patients with refractory angina. BACKGROUND Early return of reflected waves from the lower body, resulting from increased arterial stiffness, augments central aortic pressure and increases left ventricular (LV) afterload and myocardial oxygen demand. EECP acutely enhances coronary perfusion (supply) and reduces LV afterload (demand). However, the mechanisms responsible for the sustained beneficial effects of EECP treatment are unclear. METHODS Radial artery pressure waveforms were recorded by applanation tonometry and central aortic pressure waveforms generated using a mathematical transfer function in 20 patients with stable refractory angina. Data were collected before and after 34 1-h EECP sessions. Augmentation index (AI\textsubscript{a}) and timing of the reflected pressure wave were calculated from the aortic waveform. RESULTS EECP treatment caused a decline in AI\textsubscript{a} and an increase in reflected wave travel time. These modifications in wave reflection characteristics caused a decrease in aortic systolic pressure and wasted LV pressure energy. The average number of angina episodes and Canadian Cardiovascular Society (CCS) class, both decreased in concordance with the physiologic changes due to EECP treatment. CONCLUSIONS EECP treatment reduces arterial stiffness and improves wave reflection characteristics in patients with refractory angina. These changes decrease LV afterload and myocardial oxygen demand and reduce the number of angina episodes, therefore enabling patients to participate in continuous exercise programs which in turn may provide long-term benefits and sustained improved quality of life.

This study analyzed the acute effects of enhanced external counterpulsation (EECP) on oxygen uptake (VO2) 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 VO2 during an EECP treatment session has not been previously reported. We measured VO2 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. VO2 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/m2, p = 0.027) and percent body fat (37 +/- 7% vs 21 +/- 9%, p = 0.006). VO2 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 VO2 during EECP treatment (CAD +0.66 +/- 0.56 ml/kg/min, p < 0.005; healthy +0.72 +/- 0.40 ml/kg/min, p < 0.001; CAD vs healthy, p = 0.13), which returned to baseline levels during recovery. In conclusion, VO2 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.


BACKGROUND Enhanced external counterpulsation (EECP) is a noninvasive, pneumatic technique that provides favorable effects in patients with coronary artery disease and heart failure. The mechanisms by which EECP exerts its beneficial effects remain poorly understood. Cyclic GMP (cGMP) regulates vascular smooth muscle tone that may improve arterial function. We investigated the effect of a single session of EECP on plasma and platelet cGMP in asymptomatic subjects with cardiovascular risk factors (HCVR) and in patients with coronary artery disease (CAD). METHODS Fifty-five subjects were included (25 HCVR and 30 CAD) and randomized into two groups to receive either sham (control) or active EECP during 1 h. Plasma and platelet cGMP were measured immediately before and after EECP by radioimmunoassay. RESULTS One hour of EECP increased cGMP plasma concentration by 52% +/- 66% (SD) (P < .001) and platelet content by 19% +/- 28% (P < .01). The increase in plasma cGMP was particularly marked in CAD patients receiving active EECP (P < .01), mainly in those with low LDL-cholesterol. Platelets, inhibition of nitric oxide synthesis by N(G)-monomethyl-L-arginine (L-NMMA) reduced cGMP by 23% +/- 31% (P < .001), whereas presence of superoxide dismutase and inhibition of phosphodiesterase-5 increased cGMP by 46% +/- 49% and 70% +/- 77%, respectively (P < .001). In all of the cases EECP increased additional platelet cGMP content, which suggests nitric oxide synthase activation. CONCLUSIONS Acute external counterpulsation showed that very early treatment increases the cGMP production that may participate in the mechanism by which EECP exerts its clinical benefit. Analysis of the modulation of platelet cGMP content suggests that EECP activated the nitric oxide-dependent pathways.


Patients with refractory angina are those for whom medical therapy has failed to eradicate the angina completely and who have persistent symptoms that are stable but limit their activities of daily living. Approach to management must include the elimination of the secondary causes of this condition and maximum medical therapy, and if angina persists, the consideration of other strategies. Controversy exists regarding the value of transmural myocardial laser revascularization. Enhanced external counterpulsation is clinically effective in approximately 70% of patients. Spinal cord stimulation is not being used clinically in the United States. In the United States, it is still an investigational procedure that is currently being evaluated prospectively in a randomized trial. Ranolazine, an inhibitor of sodium-dependent calcium overload, may prove to be useful in patients with refractory angina.
Enhanced external counterpulsation (EECP) significantly augments diastolic blood flow and has been postulated to improve endothelial function by increased shear stress. We examined the effects of EECP on plasma nitric oxide and endothelin-1 (ET-1) levels. Plasma nitrate and nitrite (NOx) and ET-1 levels were measured serially in 13 patients with coronary artery disease who received 1-hour daily treatments of EECP over 6 weeks. During the course of EECP therapy, plasma NOx progressively increased and plasma ET-1 progressively decreased. After 36 hours of EECP, there was a 62 ±17% increase in plasma NOx compared with baseline (43.6 ± 4.3 vs 271±2.6 micromol/L, p <0.0001) and a 36 ± 8% decrease in plasma ET-1 (76.7 ± 9.5 vs 119.5 ± 8.5 pg/L, p <0.0001). At 3 months after completion of EECP, NOx remained 12±11% above baseline (p = 0.002), and ET-1 remained 11 ±10% below baseline (p = 0.0068). Our data provides neurohormonal evidence to support the hypothesis that EECP improves endothelial function.

Background: Enhanced external counterpulsation (EECP) is a non-invasive technique that has been shown to be effective in reducing both angina and myocardial ischemia in patients not responding to medical therapy and without revascularization alternatives. The aim of the present study was to assess the long-term outcome of EECP treatment at a Scandinavian centre, in relieving angina in patients with chronic refractory angina pectoris. Methods: 55 patients were treated with EECP. Canadian cardiovascular society (CCS) class, antianginal medication and adverse clinical events were collected prior to EECP, at the end of the treatment, and at six and 12 months after EECP treatment. Clinical signs and symptoms were recorded. Results: EECP treatment significantly improved the CCS class in 79 ± 6% of the patients with chronic angina pectoris (p < 0.001). The reduction in CCS angina class was seen in patients with CCS class III and IV and persisted 12 months after EECP treatment. There was no significant relief in angina in patients with CCS class II prior to EECP treatment. 73 ± 7% of the patients with a reduction in CCS class after EECP treatment improved one CCS class, and 22 ± 7% of the patients improved two CCS classes. The improvement of two CCS classes could progress over a six months period and tended to be more prominent in patients with CCS class IV. In accordance with the reduction in CCS classes there was a significant decrease in the weekly nitroglycerin usage (p< 0.05). Conclusion: The results from the present study show that EECP is a safe treatment for highly symptomatic patients with refractory angina. The beneficial effects were sustained during a 12-months follow-up period.

Enhanced external counterpulsation (EECP) is a recently approved treatment modality for patients with angina and heart failure. However, the efficacy of EECP on left ventricular (LV) function has not been well established. The study was aimed to determine whether EECP leads to an improvement in objective parameters of LV function. Patients with coronary artery disease (n = 10) who showed evidence of stress-induced myocardial ischemia despite conventional medical or surgical therapies were enrolled and received EECP therapy for a total of 35 h. The therapeutic effects of EECP were examined by thallium-201 single-photon emission computed tomography (201TI-SPECT). Compared with baseline, the lung/heart ratio at stress decreased significantly from 0.40 +/- 0.08 to 0.35 +/- 0.08 (p = 0.001) at 1 month and 0.33 +/- 0.10 (p = 0.03) at 6 months following EECP treatment. LV ejection fraction marginally improved from 56.7 +/- 7.7% to 57.6 +/- 5.9% (p = 0.382) at 1 month and to 60.1 +/- 8.6% (p = 0.062) at 6 months after EECP therapy, although not statistically significant. We concluded that EECP improved LV function, shown as the reduction of lung/heart ratio at stress, in patients with coronary artery disease, up to 6 months after EECP treatment.

OBJECTIVE Enhanced external counterpulsation (EECP) is a noninvasive, well-tolerated treatment, effective for managing patients with refractory angina pectoris. The aim of this study was to evaluate the efficacy of EECP to relieve symptoms, to decrease myocardial ischaemia and to improve cardiac performance in patients with intractable angina, refractory to surgical and medical treatment.

METHODS Twenty-five patients (24 men and one woman, mean age 65 years) with persistent ischaemia notwithstanding optimal medical therapy or after interventional or surgical procedure received EECP sessions for 35 h. Each patient underwent dobutamine stress echocardiography before and after treatment. We evaluated modifications in either cardiac systolic or diastolic function, and in wall motion score index. RESULTS Eighty-four percent of patients showed an increase in at least one functional angina class. We did not observe any significant changes in fractional shortening and diastolic function. Thirty-six percent of patients had a reduction in the area of inducible ischaemia at dobutamine stress echocardiography after treatment. Unfortunately, because of the small sample size, we did not find any statistically significant difference. There was a trend showing that patients who benefited the most were those with the worst systolic function and with severely compromised segmental kinesis (P = NS).

CONCLUSIONS EECP is effective in relieving symptoms in patients with refractory angina and may reduce inducible ischaemia at dobutamine stress echocardiography, especially in patients with reduced systolic function and compromised segmental kinesis.


Balloon counterpulsation has gained widespread acceptance as a therapy for cardiogenic shock. However, over the past four decades a parallel method of noninvasive counterpulsation, enhanced external counterpulsation (EECP), has been defined and developed. Mechanisms of benefit for this technology continue to emerge and include enhanced coronary and other key target organ perfusion beds. Other mechanisms include angiogenesis and enhanced cellular metabolism. Beyond putative mechanisms there is ample evidence for improved and sustained outcomes in patients with and without left ventricular dysfunction. This evidence comes from long-term registry reports and randomized clinical trials. With respect to heart failure (HF), there is registry, pilot trial, and randomized clinical trial evidence of safety and efficacy. This paper summarizes some of the mechanisms and outcomes of EECP in HF patients and helps to elucidate the role of EECP in the management of patients with chronic HF.


BACKGROUND Treatment of angina recalcitrant to conventional pharmacological therapy and revascularization remains problematic. Safe, effective and affordable treatments with high patient acceptability are desirable. Enhanced external counterpulsation (EECP) may fulfill these criteria better than many other proposed interventions. OBJECTIVE To examine the immediate and long-term effect of EECP in treatment of chronic stable refractory angina. DESIGN Prospective observational study of consecutive patients treated with EECP and follow-up for 1 year. MAIN OUTCOME MEASURES Canadian Cardiovascular Society (CCS) angina grading, weekly angina frequency and glyceryl trinitrate (GTN) use. RESULTS Sixty-one patients were treated with EECP and 58 completed a course of treatment. Further analysis is confined to those who completed EECP. About 52% of patients suffered from CCS III and IV angina prior to EECP. Immediately post-EECP, angina improved by at least one CCS class in 86% and by two classes in 59%. At 1-year follow-up, sustained improvement in CCS was observed in 78% of the patients. The median weekly angina frequency and GTN use were significantly reduced immediately after EECP [7 (4-14) vs. 1 (0-4) episodes per week and 7 (2-16) vs. 0 (0-2) times per week respectively, p<0.0001; data in median (interquartile range)]. The reduction was sustained at 1-
year follow-up. In 48 patients, their mean exercise time improved significantly after EECP [301 +/- 130 s vs. 379 +/- 147 s, p<0.0001]. Major adverse treatment-related events were rare. CONCLUSION This study shows that for patients who fail to respond to conventional measures, a high proportion gain symptomatic benefit from EECP.


BACKGROUND In the International Enhanced External Counterpulsation Patient Registry (IEPR), approximately 85% of the patients treated are in Canadian Cardiovascular Society (CCS) class III-IV with no option for further invasive coronary revascularization procedures. HYPOTHESIS This study sought to determine whether it is clinically important to establish whether the observed durable reduction in disabling severe angina with enhanced external counterpulsation (EECP) treatment can be extended to those with less severe CCS class II angina, who also have no option for further revascularization.

METHODS This study evaluated the immediate response, durability and clinical events over a 2-year period after EECP treatment in 112 patients with Canadian Cardiovascular Society (CCS) class II angina versus 1346 patients with class III-IV angina using data from the International EECP Patient Registry (IEPR).

RESULTS Treatment with EECP significantly (by at least one CCS class) reduced angina frequency, nitroglycerin use, and improved quality of life in both groups. At 2-year follow-up, 74% of class II and 70% of class III-IV patients remained free of major adverse cardiovascular events (MACE) and continued to demonstrate a durable CCS class improvement over baseline. CONCLUSION The robust effectiveness of EECP as a noninvasive device, together with its relatively low start-up and recurrent costs, makes it an attractive consideration for treating patients with milder refractory angina in addition to the patient with severely disabling angina treated in current practice.


Enhanced external counterpulsation (EECP) is a noninvasive circulatory assist device that has recently emerged as a treatment option for refractory angina in left ventricular (LV) dysfunction. This 2-year cohort study describes the long-term follow-up of patients who had severe LV dysfunction that was treated with EECP for angina pectoris and reports clinical outcomes, event-free survival rates, and the incidence of repeat EECP. This study included 363 patients who had refractory angina and LV ejection fraction < or =35%. Most patients reported quality of life as poor. After completion of treatment, there was a significant decrease in severity of angina class (p < 0.001), and 72% improved from severe angina to no angina or mild angina. Fifty-two percent of patients discontinued nitroglycerin use. Quality of life improved substantially. At 2 years this decrease in angina was maintained in 55% of patients. The 2-year survival rate was 83%, and the major adverse cardiovascular event-free survival rate was 70%. Forty-three percent had no reported cardiac hospitalization; 81% had no reported congestive heart failure events. Repeat EECP was performed in 20% of these patients. The only significant independent predictor of repeat EECP in a proportional hazard model was failure to complete the first EECP treatment course (hazard ratio 2.9, 95% confidence interval 1.7 to 4.9). Improvements in angina symptoms and quality of life were maintained at 2 years. In conclusion, for patients who have high-risk LV dysfunction, EECP offers an effective, durable therapeutic approach for refractory angina. Decreased angina and improvement in quality of life were maintained at 2 years, with modest repeat EECP and low major cardiovascular event rates.

OBJECTIVES We evaluated the association of baseline body mass index (BMI) on the outcomes of enhanced external counterpulsation (EECP) therapy for chronic stable angina. BACKGROUND We are in the midst of a pandemic of obesity, which is complicating the care of patients with coronary artery disease (CAD). METHODS We examined 2730 patients enrolled from 2002 to 2004 in the IEPR-2. Baseline and outcome variables were stratified by the entry BMI in kilograms per meter squared. RESULTS Obesity (BMI > 30 kg/m2) was common (40.6%) among patients with severe CAD referred for EECP. Within the total cohort, 2.6% was underweight (BMI < or = 20 kg/m2) and 4.5% was morbidly obese (BMI > 40 kg/m2). Prevalence of diabetes, hypertension, dyslipidemia, and heart failure (HF) was higher in obese patients. However, the rates of baseline angina and prior revascularization were similar among the groups. The peak diastolic augmentation ratio was similar between groups during the first (0.7 ± 0.4 for lowest and highest BMI) and last hours of treatment (0.9 +/- 0.5 and 0.8 +/- 0.5). The cumulative hours of treatment, the change in angina class, and the Duke Activity Status Index were similar for all BMI groups. There was a greater reduction in weekly anginal episodes from baseline across ascending levels of BMI (-6.3 ± 13.6 to -9.7 ±15.8, P = .03). The rates of discontinuation for clinical events were highest (14.3%) with skin breakdown being the most frequent cause (10.1%) in the underweight. The rates of clinical events including myocardial infarction, HF, and death trended higher across ascending levels of BMI (P = .52). Multivariate analysis found that older age, history of stroke, history of HF, and diabetes, but not BMI, were predictors of clinical events. CONCLUSIONS More than 40% of patients with severe CAD referred for EECP were obese. Underweight patients had higher rates of discontinuation of treatment mainly because of skin breakdown. Symptomatic benefit of EECP was similar among all BMI groups. However, despite symptomatic improvement, there was a nonsignificant trend for higher rates of myocardial infarction, HF, and death as BMI increased.

2005


Enhanced external counterpulsation (EECP) is an effective noninvasive treatment of coronary artery disease. Its mechanism of action remains unknown. An acute coronary occlusion dog model was created to explore the angiogenic effect of EECP. After coronary occlusion, 12 dogs were randomly assigned to either EECP (n = 6) or control (n = 6). Immunohistochemical studies of alpha-actin and von Willebrand factor (vWF) were used to detect newly developed microvessels. Systemic and local vascular endothelial growth factor (VEGF) were identified by ELISA and reverse transcriptase PCR analysis. There was a significant increase in the density of microvessels per squared micrometer in the infarcted regions of the EECP group compared with the control group (vWF, 15.2 +/- 6.3 vs. 4.9 ± 2.1, p<0.05; alpha-actin, 11.8 ± 5.3 vs. 3.4 ± 1.2, p<0.05). The positive-stained area per squared micrometer also increased significantly (alpha-actin, 6.6 x 10 (3) ± 2.9 x 10 (3) microm2 vs. 0.6 x 10 (3) ± 0.5 x 10 (3) microm2, p<0.05; vWF, 5.7 x 10 (3) ± 1.9 x 10 (3) microm2 vs. 1.7 x 10 (3) ± 1.4 x 10 (3) microm2, p<0.05). Immunohistochemical staining and reverse transcriptase PCR analysis documented a significant increase in VEGF expression. These factors associated with angiogenesis corresponded to improved myocardial perfusion by 99mTc-sestamibi single-photon emission computed tomography. Angiogenesis may be a mechanism of action for the improved myocardial perfusion demonstrated after EECP therapy.


BACKGROUND Enhanced external counterpulsation (EECP) reduces angina and extends time to exercise-induced ischemia in patients with symptomatic coronary disease. One- and two-center studies and a retrospective case series reported that EECP improves myocardial perfusion in stable angina pectoris. We sought to critically evaluate and quantify the effect of EECP on myocardial perfusion.
METHODS In 6 US university hospitals, EECP was performed for 35 hours in patients with class II to IV angina who had exercise-induced myocardial ischemia. Symptom-limited quantitative gated technetium Tc 99m sestamibi single photon emission computed tomography exercise perfusion imaging was performed at baseline and 1 month post-EECP. Sestamibi was injected at the same heart rate in both stress tests. Single photon emission computed tomography exercise perfusion imaging was read at a blinded core laboratory. RESULTS Thirty-seven patients were enrolled, 34 of whom completed pre- and post-EECP stress testing. The mean age was 61 +/- 10 years, 81% were male, 78% had prior revascularization, and 68% had 3-vessel disease. The mean angina class decreased from 2.7 +/- 0.7 at baseline to 1.7 +/- 0.7 after EECP (p<0.001). Exercise duration increased from 9.1 +/- 3.7 minutes at baseline to 10.2 +/- 3.6 minutes post-EECP (p=0.03). The average percentage of tracer uptake, magnitude of reversibility, average thickening fraction, and the left ventricular ejection fraction remained unchanged after EECP. CONCLUSIONS We confirm previous report that EECP reduces angina and improves exercise capacity. There were no significant changes in mean defect magnitude, amount of reversibility, thickening fraction, and ejection fraction measured using myocardial quantitative single photon emission computed tomography imaging when compared at identical pre- and post-EECP heart rates.


BACKGROUND Enhanced external counterpulsation (EECP) has been demonstrated to be an effective method for the treatment of atherosclerotic vascular disease. However, the exact mechanism underlying the beneficial effects of EECP is not completely clear. We hypothesized that EECP leads to improvement in endothelial function, contributing to its clinical benefits. METHODS Fifteen male domestic pigs were initially divided into 2 dietary groups: one consumed a normal feeding (NF) of pig chow (n=5), and one consumed a high-fat (HF) pig chow (n=10). After 8 weeks on the NF or HF diet, 5 HF pigs received EECP treatment (HF+EECP) 1 h daily for 6 weeks and the remaining 5 HF pigs continued to be fed by high cholesterol diet. At the end of 6-week EECP treatment, the carotid arterial rings from all of the pigs were harvested. Endothelium-dependent and -independent vasorelaxation to acetylcholine (ACh) and sodium nitroprusside (SNP) were measured in a dose-dependent manner. RESULTS The high fat diet resulted in increase in plasma cholesterol and triglyceride levels (p<0.05). Endothelium-dependent vasorelaxation was decreased in the HF group compared to the NF control (p<0.05). However, EECP treatment partially improved impaired endothelium-dependent vasorelaxation in the HF+EECP group compared to the HF control (p<0.05). Endothelium-independent vasorelaxation was not significantly different among the three groups. CONCLUSIONS Endothelium-dependent vasorelaxation is impaired in the hypercholesterolemic pigs. EECP treatment significantly improves hypercholesterolemia-induced diminished endothelium-dependent vasorelaxation. It suggests that amelioration in endothelial function may at least in part contribute to the beneficial effects of EECP treatment in clinical practice.


BACKGROUND Enhanced external counterpulsation (EECP), a noninvasive treatment for patients with angina pectoris, provides long-term benefits of decreased anginal frequency and improved exercise tolerance. Previous studies have suggested that shear stress may result in angiogenesis and alter endothelial hemostatic factor release. Whether EECP therapy effects an alteration in endothelial cell proliferation and function remains unclear. The level of vascular endothelial growth factor (VEGF) and four other endothelial hemostatic factors (tissue plasminogen activator, plasminogen activator inhibitor-1, von Willebrand factor, and D-dimers) were measured in patients before and after 35 hours of EECP treatment. METHODS Plasma levels of endothelial growth and hemostatic factors were assessed using the standard enzyme-linked immunosorbent method. RESULTS No significant difference in the hemostatic factors and VEGF after EECP treatment was revealed; there was a trend toward an increase in VEGF levels post- treatment. CONCLUSIONS Vascular endothelial cells play a critical role in the regulation of coagulation because they control the expression of tissue plasminogen activator,
plasminogen activator inhibitor-1, von Willebrand factor, and D-dimers. Our results suggest EECP may not play a role in controlling coagulation in patients with coronary artery disease through release of endothelial hemostatic factors. Although there was a tendency for increased VEGF release, larger studies are necessary to confirm these observations.


The basic principle of enhanced external counterpulsation (EECP) is diastolic augmentation of arterial pressure, lowering of systolic arterial pressure along with increasing venous return. EECP is a noninvasive procedure involving sequential inflation and rapid deflation of compressive cuffs wrapped around the patient's calves, thighs, and lower abdomen, timed to the cardiac cycle using the electrocardiogram. Theoretically, this should result in decreased myocardial oxygen demand and an increased coronary blood flow. Long-term benefits may be the result of the opening of dormant coronary collateral circulation, but this is theory and not proven. Extracardiac factors, such as peripheral arterial stiffness, endothelial dysfunction, and elevated myocardial oxygen demand, are also the therapeutic targets for EECP. There is some evidence that long-term benefits may be the result of a training effect due to 35 1-hour diastolic inflations at 300 mm Hg and systolic deflations of the compressive cuffs. To date, the extracardiac effects of EECP have received little attention and peripheral vascular adaptations to EECP have not been investigated. EECP, by promoting lower-extremity arterial "run-off" and intermittent reactive hyperemia in the legs with each inflation/deflation cycle of the compressive cuffs, may improve peripheral vascular function, thus inducing changes in peripheral vascular biology that will reduce ventricular work and myocardial oxygen demand in patients with coronary artery disease similar to that of exercise. At the University of Florida, this therapy is used for patients with chronic stable angina who are refractory to medical therapy and are not candidates for a revascularization procedure. The treatment does take time (35 once-a-day 1-hour treatments), and not all patients are candidates for the procedure. For example, patients with severe peripheral vascular disease, severe hypertension, thrombophlebitis, markedly irregular heart rhythm, and severe aorta insufficiency are excluded. Approximately 75% of patients report improvement (ie, a decrease in symptoms and an increase in exercise duration). Our results are such that this management strategy does deserve consideration in patients with persistent chronic stable angina on maximum medical therapy who are not candidates for revascularization and are unhappy with their lifestyle.


Enhanced external counterpulsation (EECP) has been shown to reduce Canadian Cardiovascular Society angina class. This study examines the factors that affect the reduction at 1 year, especially in patients who do not demonstrate an initial response. The data of 2,007 consecutive patients enrolled in the International EECP Patient Registry were analyzed. After 36.6 +/- 4.9 h of EECP, angina was reduced by at least one class in 82.7%. At 1 year, 35.4% of initial nonresponders and 70.6% of responders remained improved by at least one angina class and free of major adverse cardiovascular events. Multivariate predictors of 1-year benefit are initial response to treatment (odds ratio 4.5, 95% CI 3.5-5.8), baseline angina class compared with class IV (odds ratios: class I 2.1, CI 0.93-4.81; class II 0.62, CI 0.43-0.87; class III 0.80, CI 0.62-1.01) and no history of congestive heart failure (odds ratio 1.41, CI 1.14-1.74).


Background Enhanced external counterpulsation (EECP) treatment can improve exercise tolerance in patients with ischemic heart disease; however, the possible benefits of EECP in patients with stable heart failure (HF) and left ventricular dysfunction (LVD) are unclear. An open pilot study showed significant increases in exercise tolerance in HF patients undergoing EECP. Thus a larger, controlled study of
EECP in patients with stable HF (New York Heart Association [NYHA] classes II and III) and LVD was undertaken. Methods and Results The PEECH trial is a controlled, randomized, single-blind, parallel-group, multicenter study of 187 patients with symptomatic but stable HF (NYHA classes II and III) and an LV ejection fraction <35% was designed to assess the efficiency of EECP in patients with stable HF. Medical therapy is optimized in all patients based on the recommendations of the Heart Failure Society of America (“Usual Care”), and then randomized between 2 treatment groups; UC or EECP (35 hours over 7 weeks). Conclusion Efficacy measures include standard exercise tolerance tests on a treadmill (modified Naughton protocol), with measurements of peak oxygen uptake and exercise duration time; quality of life questionnaires; NYHA classification; and neurohormonal markers of HF.


Method 14 consecutive patients with coronary artery disease and refractory angina pectoris were selected for EECP treatment if they met the following criteria: (1) age between 21 and 81 years; (2) symptoms consistent with Canadian Cardiovascular Society Classification angina levels I, II or III; (3) documented evidence of coronary artery disease; and (4) exercise treadmill test (ETT) positive for ischemia. Patients were excluded if they had medical conditions that contraindicated EECP or that might interfere with study. The subjects received 35 hours of EECP treatment. All patients underwent resting and dobutamine stress echocardiography (DSE) before and after EECP therapy. Two-dimensional and Doppler echocardiography examinations were performed with Acuson Sequoia machines (Mountain View, CA) equipped with a variable-frequency phased-array transducer (2.5 to 3.5 to 4.0 MHz).

Results All patients experienced an increase in LVEF at both rest and peak stress as a result of EECP treatment. Mean resting LVEF increased from 47.2% before EECP to 52.1% after EECP (p < 0.000001). Mean peak stress LVEF increased from 65.3% before EECP to 70.3% after EECP (p<0.000001). No statistically significant difference was observed for any of the diastolic parameters. Conclusion The present study demonstrated that even in the presence of normal to mild left ventricular dysfunction, EECP augmented EF from 47% to 52% at rest and from 65% to 70% at peak exercise without alteration in systolic blood pressure and heart rate. Therefore, EECP treatment may have a positive effect on systolic function, but its effect on diastolic function must be elaborated in larger studies. Preliminary data from clinical studies show that EECP represents a safe and effective treatment in patients with impaired left ventricular function. The salutary response seen in these studies may in part have been mediated by augmenting systolic function.


BACKGROUND AND PURPOSE Enhanced external counter pulsation (EECP) is used to treat angina. With sustained treatment this increases collateral circulation to the coronary arteries as well as to the body as a whole. We found some patients who underwent EECP for angina or congestive heart failure who also coincidentally had severe Restless Legs Syndrome (RLS). Case reports are presented.

PATIENTS AND METHODS Six patients with RLS (1F, 5M, ages 55-80) underwent EECP treatment. All patients were given the International RLS Study Group rating scale for RLS (the IRLS) before and immediately after 35 days of EECP treatment. RESULTS The average IRLS rating scale score of the six patients before treatment was 28.8 (range 23-35), which indicates frequent and moderate to very severe RLS. After 35 days of EECP treatment the IRLS score was 6 (P<0.03), which indicates clinically insignificant RLS. Long-term follow-up in three patients indicates sustained improvement in all three at 3-6 months after EECP was completed (IRLS score 28.3-3.33). Further follow-up in four patients showed sustained improvement in two patients 1 year after EECP was completed. CONCLUSION EECP improves RLS symptoms significantly and could be considered as an adjunct treatment for patients with RLS. In some cases, the improvement lasts for months after the course of treatment. In this way EECP is
unique and unlike pharmacotherapy which requires continuous daily treatment. Furthermore, our results suggest that decreases in vascular flow influence the peripheral or central nervous system leading to the sensory symptoms of RLS. A larger number of patients studied under blinded conditions is needed to draw further conclusions.


The development of advanced revascularization techniques has resulted in the growth of a subset of patients with coronary artery disease who are nonrevascularizable and are considered to have refractory angina. Enhanced external counterpulsation (EECP) has been developed for the management of these patients with chronic, refractory disease. Evidence has shown that through improvement of vascular endothelial function and recruitment of collateral vessels, EECP provides many clinical benefits. These patients experience sustained decreases in angina, improvement in exercise time, improved myocardial perfusion, and enhanced quality of life. Furthermore, EECP appears to be safe and effective in the treatment of angina in patients with impaired systolic function and has similar potential in patients with congestive heart failure.


BACKGROUND Advanced liver cirrhosis is characterized by cardiovascular changes, such as low arterial blood pressure, peripheral vasodilation and renal vasoconstriction. As a consequence, renal hypoperfusion, impaired diuresis and natriuresis and eventual hepatorenal syndrome may ensue. Previous studies using head-out water immersion to increase central blood volume have demonstrated the functional nature of the renal abnormalities. Enhanced external counterpulsation (EECP) is a new non-invasive cardiac assist device to augment diastolic blood pressure by electrocardiogram-triggered diastolic inflation and deflation of cuffs wrapped around the lower extremities. We investigated whether EECP would improve renal dysfunction of liver cirrhosis. METHODS Twelve healthy controls and 19 patients with liver cirrhosis were observed during 2 h of baseline followed by 2 h of EECP. The following parameters of renal and cardiovascular function were measured: renal plasma flow by paraaminohippurate clearance, glomerular filtration rate (GFR) by inulin clearance, urine flow rate, urinary excretion rates of sodium and chloride, mean arterial blood pressure (MAP), renal vascular resistance (RVR) and plasma concentrations of renin, atrial natriuretic peptide (ANP), endothelin-1, antidiuretic hormone, epinephrine and N-epinephrine. RESULTS EECP was well tolerated by healthy controls and cirrhotic patients alike. EECP increased MAP (cirrhotic patients: from 74+/−18 to 88+/−20 mmHg, P<0.01; controls: from 89+/−8 to 94+/−5 mmHg, p=NS) and ANP (cirrhotic patients: from 23+/−18 to 30+/−20 ng/l, p<0.05; controls: from 11+/−4 to 16+/−5 ng/l, p<0.01). The plasma renin concentration decreased (cirrhotic patients: from 98+/−98 to 58+/−57 ng/l, p<0.01; controls: from 4.6+/−1.6 to 3.4+/−1.1 ng/l, p<0.01). This was associated with improvement of the urinary flow rate (cirrhotic patients: from 3.6+/−1.8 to 4.6+/−0.7 ml/min, p<0.05; controls: from 1.8+/−1.5 to 2.8+/−1.9 ml/min, p<0.05), as well as of the sodium and chloride excretion rates in both groups. However, in contrast to healthy controls, GFR and renal plasma flow in cirrhotic patients failed to rise significantly. Renal vascular resistance fell numerically in healthy controls (68+/−5 vs 55+/−4 mmHg . min/l; p=NS). In contrast, RVR showed a significant increase by approximately 20% in cirrhosis (67+/−4 vs 80+/−8 mmHg . min/l; p<0.05). Endothelin-1 levels fell in controls (0.38+/−0.42 vs 0.31+/−0.35; p<0.05), whereas they remained statistically unchanged in cirrhotic patients. Epinephrine, N-epinephrine and vasopressin were not altered by EECP in either group. CONCLUSIONS EECP is an effective procedure to augment renal excretory function in healthy volunteers as well as in patients with cirrhosis. In healthy volunteers, GFR and renal plasma flow increased during EECP. In contrast, these parameters remained unchanged in the patients and their renal vascular resistance increased during EECP. Therefore, EECP improves diuresis, but does not influence the vasoconstrictive dysregulation of the kidneys in liver cirrhosis.

- Lawson WE, Silver MA, Hui JCK, Kennard ED, Kelsey SF. Angina Patients with Diastolic Versus Systolic Heart Failure Demonstrate Comparable Immediate and One-Year Benefit...
BACKGROUND Enhanced external counterpulsation (EECP) is effective in treating angina in coronary artery disease patients. Whether EECP produces similar immediate and sustained benefits and freedom from adverse events (MACE) at 1 year in patients with severe systolic dysfunction versus diastolic dysfunction is unknown. METHODS AND RESULTS Data of 746 angina patients with a history of heart failure enrolled in the International EECP Registry were divided into 2 groups: left ventricular ejection fraction (LVEF) < or =35% (S) and LVEF >35% (D). Mean LVEF was 51.0 +/- 10.2% in diastolic dysfunction (n=391) versus 26.3 +/- 6.9% in systolic dysfunction (n=355). At baseline, 92.0% of diastolic dysfunction and 90.9% of systolic had Canadian Cardiovascular Society Class III/IV angina with similar number of anginal episodes and nitroglycerin use. After 32 hours of EECP, angina was reduced by > or =1 class in 71.9% of diastolic versus 72.2% of systolic with similar decreases in anginal episodes and nitroglycerin use. At 1-year 78.1% of diastolic and 75.8% of systolic had less angina than pre-EECP. MACE at 1 year was also comparable (24.4 versus 23.8%). CONCLUSIONS The benefits of EECP in heart failure patients were similar regardless of diastolic or systolic dysfunction. The improvement was sustained at 1 year with similar MACE.


We assessed the frequency, efficacy, predictors, and long-term success of repeat enhanced external counterpulsation (EECP) therapy in relieving angina in a large cohort of patients who had chronic angina pectoris and had undergone a full course of EECP. Within 2 years of the initial course of EECP, the rate of repeat EECP was 18%, which occurred at a mean interval of 378 days after initial EECP. Of those who underwent repeat EECP, 70% had a decrease of >1 angina class at the end of repeat EECP with similar decreases in nitroglycerin use.


OBJECTIVES Enhanced external counterpulsation (EECP) rhythmically augments blood pressure (BP) by diastolic lower-body compression. Recently, we showed decreased mean cerebral blood flow velocity (CBFVmean) in young healthy persons during EECP, but unchanged CBFVmean in atherosclerotic patients. In this study, we assessed EECP effects on dynamic cerebral autoregulation (CA).

MATERIALS & METHODS In 23 healthy persons and 15 atherosclerotic patients we monitored heart rate (HR), mean BP (BPmean) and CBFVmean before and during 5 min EECP. We analyzed spectral powers of HR, BPmean and CBFV mean in the low (LF: 0.04-0.15 Hz) and high (HF: 0.15-0.5 Hz) frequency ranges to determine CA from the LF-transfer function gain and phase shift between BPmean and CBFV mean oscillations. RESULTS EECP increased HR and BPmean, while transfer function gain and phase shift remained stable. CONCLUSIONS: Stable gain and phase values suggest that EECP does not compromise CA and, therefore, does not seem to bear cerebrovascular risks.

2004


BACKGROUND The hemodynamic effects of enhanced external counterpulsation (EECP) and its
mechanism(s) were investigated in relation to neurohumoral factors in patients with acute myocardial infarction (AMI). METHODS AND RESULTS Twenty-four patients with AMI were studied before, during and after EECP treatment for 60 min. Heart rate (HR), right atrial pressure (RAP), pulmonary capillary wedge pressure (PCWP) and cardiac index (CI) were determined. In addition, circulating concentrations of neurohumoral factors were determined at each time point. HR did not change following EECP treatment. However, RAP and PCWP increased significantly and CI was significantly elevated during EECP and thereafter. Blood atrial natriuretic peptide (ANP) concentration was significantly increased 15 and 60 min after the start of EECP treatment, but brain natriuretic peptide (BNP) did not change. Renin, aldosterone and catecholamine concentrations also did not change. CONCLUSION Treatment with EECP resulted in an increased preload because of increased venous return, and CI was increased thereafter. In patients with AMI, EECP increased blood ANP concentration, but not BNP, which suggests that an increase in ANP without an increase in BNP is an important mechanism for the effects of EECP treatment.


Angina pectoris is a debilitating indication of the presence of ischemic heart disease that affects millions of Americans. Although a number of pharmacologic treatments are available, the annual number of revascularization surgeries continues to rise in the United States. Other management strategies, such as spinal cord stimulation, enhanced external counterpulsation, metabolic modulators, and gene therapy, are being explored.


Patients with refractory angina are not candidates for revascularization and have both class III or IV angina and objective evidence of ischemia despite optimal medical therapy. An estimated 300,000 to 900,000 patients in the United States have refractory angina, and 25,000 to 75,000 new cases are diagnosed each year. This review focuses on treatment strategies for refractory angina and includes the mechanism of action and clinical trial data for each strategy. The pharmacological agents that have been used are ranolazine, ivabradine, nicorandil, L-arginine, testosterone, and estrogen; currently, only L-arginine, testosterone, and estrogen are approved by the Food and Drug Administration. Results with the noninvasive treatments of enhanced external counterpulsation and transcutaneous electrical nerve stimulation are provided. Invasive treatment strategies including spinal cord stimulation, transmyocardial revascularization, percutaneous myocardial revascularization, and gene therapy are also reviewed.


BACKGROUND To date, no satisfactory therapy has become available for patients with acute central retinal artery occlusion (CRAO) or branch retinal artery occlusion (BRAO). Enhanced external counterpulsation (EECP) is a new noninvasive procedure that increases perfusion of inner organs. In the current study, the authors measured the impact of EECP on reperfusion in ischemic retinal tissue. METHODS In a prospective, randomized study, 20 patients with CRAO or BRAO were included. Ten patients were given hemodilution therapy and 2 hours of EECP, and 10 patients were given regular hemodilution therapy only. Quantification of changes in retinal perfusion was carried out by means of scanning laser Doppler flowmetry (in arbitrary units). RESULTS Enhanced external counterpulsation caused no observable adverse events. A significant increase in perfusion occurred immediately after EECP in the ischemic retinal areas (57 +/- 19 arbitrary units versus 99 +/- 14 arbitrary units). In contrast, no change was measured in the group not treated with EECP (83 +/- 19 arbitrary units versus 89 +/- 44 arbitrary units). Forty-eight hours later, a significant increase in perfusion could be shown in the ischemic retina of both groups, and no significant difference of perfusion was found between the two groups any
Background Enhanced external counterpulsation (EECP) is a noninvasive device that uses three pairs of sequentially inflated pneumatic cuffs applied to the lower extremities and synchronized with the heart beat to provide diastolic augmentation, increase coronary blood pressure and flow, venous return and cardiac output, and decrease afterload. Hypothesis This study examines the safety and effectiveness of EECP therapy in patients with significant left main coronary artery disease (LMD). Methods In all, 2,861 patients enrolled in the International EECP Patient Registry (IEPR) were divided into three groups, those without LMD (n = 2,377), those with LMD and prior CABG (n = 431), and those with unbypassed LMD (n = 53). Results Patients with LMD, with or without prior CABG, were significantly more likely to have triple-vessel disease (98.1 and 88.7%, respectively) than patients without LMD (41.9%). Post-EECP, 74% without LMD, 75% with LMD with prior CABG, and 65% with unbypassed LMD improved their Canadian Cardiovascular Society (CCS) angina by at least one class (p = NS). There were no differences in the mean decrease in weekly angina episodes (7.1 vs. 8.0 vs. 7.6) and in the mean frequency of weekly nitroglycerin use (6.6 vs. 8.1 vs. 8.9). At 6-month follow-up, the CCS class improved further in all three groups, and there was a further reduction in mean weekly angina episodes (4.7 vs. 4.6 vs. 5.3) and nitroglycerin use (6.5 vs. 6.8 vs. 8.2). Kaplan-Meier life table analysis 8 months after starting EECP demonstrated a major cardiovascular event rate of 11.2% in patients without LMD, 15.6% in LMD with CABG, and 24.3% in LMD without prior CABG. Late mortality in unbypassed LMD was 13.2% (confidence interval [CI] 3.3–23.1) versus 4.8% (CI 2.7–7.1) in LMD with CABG, and 2.8% (CI 2.1–3.5) without LMD (p = 0.0039 by log-rank test). Conclusion Enhanced external counterpulsation is equally effective in relieving angina in patients with or without LMD. However, the significantly increased late mortality in patients with LMD without prior CABG suggests that early revascularization should be considered in these patients.


Background Enhanced external counterpulsation therapy (EECP), in addition to improving coronary flow and increasing the time to ischemia, noninvasively alters hemodynamics in patients with severe coronary artery disease (CAD). Other treatments that alter hemodynamics, for example, balloon valvuloplasty, left ventricular assist devices, and pharmacologic antagonism of the rennin-angiotensin system, promote electrophysiologic remodeling, as evidenced by alterations in the QT interval. METHODS We studied 28 patients who completed a 7-week, 35-hour session of EECP to assess whether such therapy would also result in electrophysiologic remodeling. RESULTS All patients had class II-III angina, imaging-proven ischemia, and severe, near-inoperable CAD. Of 28 patients, with a mean age 62 +/- 13 years (mean +/- SD), 78% were male, 46% diabetic, 82% hypertensive, 60% had undergone angioplasty, and 67% had undergone bypass surgery. The mean ejection fraction was 44% (range 25-60%). Following EECP, most patients (82%) had at least a one full class improvement in their anginal pattern. In most patients, there was substantial baseline conduction system disease present: a mean QRS of 105 +/- 19 ms. It is to be noted that there was no significant change in heart rate (HR), PR, QRS, or QT(c) intervals before and after EECP in either clinical responders or nonresponders. When analyzed by response to EECP, ejection fraction, or history of revascularization, there were still no detectable changes in ECG parameters (all P = NS). CONCLUSIONS While EECP remains an effective treatment for severe CAD, it does not prompt early electrical remodeling of the heart.

• **Lawson WE, Hui JCK, Barsness GW, Kennard ED, Kelsey SF for the IEPR Investigators. Effectiveness of Enhanced External Counterpulsation in Patients with Left Main Disease and Angina. Clinical Cardiology. 2004 Aug;27(8):459-463.**
BACKGROUND Enhanced external counterpulsation (EECP) augments diastolic and reduces systolic blood pressures. Enhanced external counterpulsation has been shown to improve blood flow in various organ systems. Beneficial effects on skin perfusion might allow EECP to be used in patients with skin malperfusion problems. This study was performed to assess acute effects of EECP on superficial skin blood flow, transdermal oxygen and carbon dioxide pressures.

MATERIALS AND METHODS We monitored heart rate, blood pressure, transdermal blood flow as well as oxygen and carbon dioxide pressures in 23 young, healthy persons (28 +/- 4 years) and 15 older patients (64 +/- 7 years) with coronary artery disease before, during and 3 min after 5 min EECP. Friedman test was used to compare the results of 90-s epochs before, during and after EECP. Significance was set at P < 0.05.

RESULTS Enhanced external counterpulsation increased heart rate and mean blood pressure. During EECP, transdermal oxygen pressure and concentration of moving blood cells increased while transdermal carbon dioxide pressure and velocity of moving blood cells decreased significantly in both groups. After EECP, transdermal carbon dioxide pressure was still reduced while the other parameters returned to baseline values. CONCLUSIONS Improved skin oxygenation and carbon dioxide clearance during EECP seem to result from the increased concentration and reduced flow velocity, i.e. prolonged contact time, of erythrocytes. The increased concentration of moving blood cells and the decreased velocity of moving blood cells at both tested skin sites indicate peripheral vasodilatation.


Enhanced external counterpulsation (EECP) is a valuable therapeutic option for patients with coronary artery disease and refractory angina. Although the exact mechanisms by which this technique exerts favorable effects remain unclear, improvement in endothelial function is considered a potential mechanism contributing to the clinical benefit associated with EECP. We describe a young woman with severely symptomatic coronary endothelial dysfunction in the absence of obstructive coronary artery disease who experienced a dramatic and sustained reduction in symptoms in response to a standard 35-hour course of EECP.


Recently published clinical trial demonstrated improved exercise tolerance and quality of life after EECP for patients with New York Heart Association class II–III heart failure (average ejection fraction of 23%) secondary to ischemic or dilated cardiomyopathy. There were no significant adverse events reported. Furthermore, data from the International EECP Patient Registry show that that patients with reduced left ventricular function (< 35%) achieved similar reductions in angina as those with preserved ejection fraction. The cost is currently estimated to be US$5000–$7000 for a 35-treatment session. However, if found to be effective and safe, EECP could result in an enormous cost savings by reducing the amount of medication patients require and the occurrence of adverse events secondary to medication interactions that often result in hospital admissions.


Enhanced external counterpulsation (EECP) is noninvasive, safe, and effective for stable angina. We have reported that the development of functional collateral vessels is one of the mechanisms of EECP therapy using ammonia positron emission tomography (PET). The efficacy of heparin treatment on collateral growth is shown in several clinical studies. We evaluated whether EECP combined with intravenous heparin injection is effective for exercise capacity and oxygen metabolism of ischemic myocardium in stable angina. Eleven patients with stable angina were treated with conventional EECP therapy (C group). Seven patients with stable angina were treated with EECP therapy with 5000 IU

John CK Hui, PhD
Page 55
heparin pretreatment (H group). At baseline and after the completion of treatment H, 7 patients underwent $^{11}$C-acetate PET to examine the change in regional myocardial oxygen metabolism. Although the total treadmill exercise time was prolonged after treatment in both groups, the extent of the improvements was significantly greater in the H group compared with the C group. Although k mono, the index of regional myocardial oxygen metabolism, in the nonischemic region remained unchanged, k mono in the ischemic region increased significantly ($p << 0.05$) from 0.038 +/- 0.004 to 0.053 +/- 0.007. In conclusion, EECP with heparin pretreatment appears to be a new treatment remedy for patients with stable angina.


We studied the effect of enhanced external counterpulsation (EECP) in 23 consecutive patients with stable angina pectoris who had a positive dobutamine stress echocardiogram. After EECP, stress-induced wall motion score (WMS) improved by $> or =2$ grades in 43% of the patients ($n = 10$); the average improvement was 5.3 +/- 3.8 compared with -0.6 +/- 3.0 in the remaining 13 patients ($p = 0.007$). The diastolic/systolic augmentation ratio increased by 217% in response to the full course of EECP ($p = 0.0002$) among patients with improved WMS, and by 71% ($p = 0.004$) among the other patients; the increase was greater among patients with improved WMS than among patients with no improvement ($p = 0.01$). After EECP, Canadian Cardiovascular Society angina class improved from 3.1 +/- 0.6 to 2.2 +/- 0.7 ($p <0.0001$) in the entire group and exercise capacity increased by 73 seconds ($p = 0.0002$) in patients who were able to exercise ($n = 18$).


We assessed the long-term outcomes of enhanced external counterpulsation in relieving angina and improving the quality of life in a large cohort of patients with chronic angina pectoris. Seventy-three percent had a reduction by $> or =1$ angina class at the end of treatment, and 50% reported an improvement in the quality-of-life assessment after enhanced external counterpulsation; these results were sustained at 2-year follow-up.


Heart failure remains a significant health problem in the United States and in the world. Despite a surfeit of recent diagnostic and therapeutic advances, patients with heart failure remain inadequately helped. The overwhelming need for new and better therapies continues to stimulate scientists to investigate new technologies. Over the past several years the use of enhanced external counterpulsation as a treatment for chronic angina has steadily increased. Recently, its potential role in heart failure management has been shown. We review the role of enhanced external counterpulsation in heart failure management as an emerging noninvasive outpatient therapy.

2003

- **Fitzgerald CP, Lawson WE, Hui JCK, Kennard ED; IEPR Investigators.** Enhanced External Counterpulsation as Initial Revascularization Treatment for Angina Refractory to Medical Therapy. Cardiology. 2003 Nov;100(3):129-135.

Enhanced external counterpulsation (EECP) is effective in patients with angina refractory to medical therapy or revascularization. However, as a noninvasive treatment it should perhaps be considered the first-line treatment with invasive revascularization reserved for EECP failures or high-risk patients. The International EECP Patient Registry was used to analyze a cohort of patients with prior percutaneous coronary intervention (PCI) and/or coronary artery bypass graft (CABG) ($n = 4,454$) compared with a
group of patients (PUMPERS) who were candidates for PCI and/or CABG and chose EECP as their initial revascularization treatment \( (n = 215) \). The PUMPERS responded to treatment with EECP with decreased anginal episodes and nitroglycerin use and with improvement in their Canadian Cardiovascular Society functional class, similarly to previously revascularized patients. Treatment with EECP resulted in sustained, and often progressive, reduction in angina over the succeeding 6 months. Given the findings of this study, it is interesting to speculate on the possibility of using EECP as the primary revascularization intervention after medical therapy proves unsatisfactory.


The International EECP Patient Registry (IEPR) collects data from 60 sites on consecutive chronic angina patients treated with EECP. The Duke Activity Index (DASI), a 12 item patient completed questionnaire, was used to measure functional capacity in patients before and after a course of EECP treatment. The Canadian Cardiovascular Society Classification (CCSC) of angina was used to monitor changes in angina. The majority of patients had severe angina, had prior invasive revascularization, but were not suitable for bypass surgery or percutaneous intervention. Functional status measured by the DASI questionnaire was poor at baseline, but improved significantly after EECP treatment. Co-morbidities although predictive of low baseline DASI, were not associated with failure to achieve functional improvement.


BACKGROUND Patients with diabetes are at greater risk for coronary events, yet they are less likely to benefit from revascularization than those without diabetes. Enhanced external counterpulsation has recently emerged as a treatment option for select patients with chronic stable angina. METHODS We examined baseline characteristics, angina response, and cardiac outcomes of patients with diabetes mellitus treated with Enhanced External Counterpulsation (EECP) for chronic stable angina. Data were collected from patients enrolled in the International EECP Patient Registry (IEPR) before and after a course of EECP, and at 1 year after completion of treatment. RESULTS Of 1532 IEPR patients studied, 43% had diabetes mellitus at baseline. Patients with diabetes were experiencing, on average, 11 episodes of angina per week. Most had been revascularized with prior percutaneous coronary intervention or coronary artery bypass graft surgery (86%) and most were considered unsuitable for either additional procedure (87%). Treatment was completed as prescribed in 79% of patients (mean, 32 hours). Immediately after EECP, 69% of patients with diabetes demonstrated a reduction in angina of > or =1 Canadian Cardiovascular Society angina class. After 1 year, maintenance of angina reduction was reported in 72% of patients with diabetes. Quality of life was significantly improved. Despite a high-risk profile among the diabetic group in this study, 1-year mortality was similar to coronary intervention registry populations. CONCLUSION This study suggests that in select patients with diabetes, EECP can be a safe, effective, well-tolerated treatment option for the relief of angina.


Data from the International Enhanced External Counterpulsation (EECP) Patient Registry were analyzed To determine which patient characteristics influence improvement in angina class with EECP treatment. Patients with severe disabling angina at baseline, men, and those without a history of smoking are more likely to improve their angina class after EECP, whereas those with diabetes mellitus, prior bypass surgery, and heart failure were less likely to benefit.
• **Sinvhal RM, Gowda RM, Khan IA. Enhanced External Counterpulsation for Refractory Angina Pectoris. *Heart*; 2003 Aug;89(8):830-833.**

Enhanced external counterpulsation (EECP) is a non-invasive outpatient treatment used for angina pectoris. In patients with intractable angina refractory to aggressive surgical and medical treatment, several novel strategies are considered including EECP, transmural laser revascularization, and spinal cord stimulation. EECP produces an acute hemodynamic effect that is presumed to be similar to that produced by the invasive intra-aortic balloon pump. By applying a series of compressive cuffs sequentially from the calves to the thigh muscles upon diastole and rapidly deflating the cuffs in early systole, an increase in diastolic and decrease in systolic pressure is created. Although data indicate improvement in angina in patients undergoing EECP, the role of EECP in the treatment of angina pectoris has not yet been well defined. At present, EECP use should be limited to patients with debilitating (functional class III and IV) refractory angina pectoris who are not candidates for revascularisation, are symptomatic despite being on maximal antianginal pharmacotherapy, and have no contraindications to EECP use.


Enhanced external counterpulsation (EECP) has been shown to reduce angina and to improve objective measures of myocardial ischemia in patients with refractory angina. Prospective clinical studies and large treatment registries suggest that a course of EECP is associated with prolongation of the time to exercise-induced ST-segment depression and resolution of myocardial perfusion defects, as well as with enhanced exercise tolerance and quality of life. With a growing knowledge base supporting the safety and beneficial clinical effects associated with EECP, this therapy can be considered a valuable treatment option, particularly in patients who have exhausted traditional revascularization methods and yet remain symptomatic despite optimal medical care. However, although the concept of external counterpulsation was introduced almost four decades ago, and despite growing evidence supporting the clinical benefit and safety of this therapeutic modality, little is firmly established regarding the mechanisms responsible for the beneficial effects associated with this technique. Suggested mechanisms contributing to the clinical benefit of EECP include improvement in endothelial function, promotion of coronary collateralization, enhancement of ventricular function, peripheral effects similar to those observed with regular physical exercise, and nonspecific placebo effects. This review summarizes the current evidence for a contribution of these mechanisms to the clinical benefit associated with EECP.


BACKGROUND Enhanced external counterpulsation (EECP) has been shown to improve treadmill times and myocardial perfusion. However, improvement in perfusion defects has been demonstrated only in patients exercised to the same cardiac workload on the post-EECP as the pre-EECP stress test.

HYPOTHESIS This study was to determine the effect of EECP on exercise capacity and myocardial perfusion by comparing results of maximal exercise radionuclide testing pre- and post-EECP treatment.

METHODS This prospective study included 25 patients with angina who had performed maximal symptom-limited exercise tolerance tests (ETT) with Bruce protocol and radionuclide perfusion single-photon emission computed tomography (SPECT) study prior to and at completion of EECP treatment.

RESULTS After 35 h of EECP, 23 patients (93%) improved by at least one functional angina class. There is a significant improvement in their total treadmill times (357 ± 93 to 449 ± 97 s, p < 0.001). There was a significant change in their peak double products, from 18,891 ± 3,939 pre-EECP to 20,464 ± 4,305 post-EECP ETT (p < 0.001). Pre EECP, 16 patients had ST-segment depression on their initial ETT. After EECP, 13 of these patients (80%) either no longer had ST depression or had a significant increase in their time to ST depression (229 ± 52 to 315 ± 60 s, p < 0.001). The radionuclide perfusion scores also showed a significant reduction in ischemic segments (16.36 ± 10.52 to 14 ± 10.9, p < 0.05).
CONCLUSIONS Patients treated with EECP demonstrated a reduction in angina symptoms, improvement in exercise capacity, increase in time to ST-segment depression, and decrease in perfusion defects despite performing at a higher workload.


Objectives Intra-aortic counterpulsation is the most frequently used cardiac assist device. However, there are only few studies of the effects of counterpulsation on cerebral blood flow and these report conflicting outcomes. The new enhanced external counterpulsation (BECP) technique reproduces non-invasively the effects of intra-aortic counterpulsation. In this study, we evaluated effects of EECP on blood pressure (BP) and on cerebral flow velocity (CBFV). Subjects and methods Twenty-three healthy controls and 15 atherosclerotic patients each underwent a 5-min session of EECP. Before, during and after EECP we monitored heart rate, beat-to-beat radial artery BP and CBFV. Results EECP induced a second increase in BP and CBFV during diastole with a significant increase of mean BP and a decrease of systolic BP in patients and controls. Mean CBFV increased in both groups during the first 5 s of EECP. After 3 min of EECP, diastolic CBFV was still higher than at baseline, but systolic CBFV was lower than at baseline; mean CBFV was as low as before EECP in the patients and lower than the baseline values in the controls. Three minutes after ending EECP, mean and systolic BP were lower in the patients than the corresponding baseline values. Otherwise, CBFV and BP values did not differ from baseline in patients and controls. Conclusion Cerebral autoregulation ensures the constancy of cerebral blood flow even though EECP creates marked systemic changes. In the patients, the decrease of BP after EECP with maintained CBFV indicates an improved BP-CBFV relation and a more economic autoregulation.


OBJECTIVES The goal of this study was to examine the effect of enhanced external counterpulsation (EECP) on endothelial function. BACKGROUND Enhanced external counterpulsation improves symptoms and exercise tolerance in patients with symptomatic coronary artery disease (CAD). However, the exact mechanisms by which this technique exerts its clinical benefit are unclear. METHODS Reactive hyperemia-peripheral arterial tonometry (RH-PAT), a noninvasive method to assess peripheral endothelial function by measuring reactive hyperemic response in the finger, was performed in 23 patients with refractory angina undergoing a 35-h course of EECP. In each patient RH-PAT measurements were performed before and after the first, at midcourse, and the last EECP session. In addition, RH-PAT response was assessed one month after completion of EECP therapy; RH-PAT index, a measure of reactive hyperemia, was calculated as the ratio of the digital pulse volume during reactive hyperemia divided by that at rest. RESULTS Enhanced external counterpulsation led to symptomatic improvement (≥1 Canadian Cardiovascular Society class) in 17 (74%) patients; EECP was associated with a significant immediate increase in average RH-PAT index after each treatment (p < 0.05). In addition, average RH-PAT index at one-month follow-up was significantly higher than that before EECP therapy (p < 0.05). When patients were divided by their clinical response, RH-PAT index at one-month follow-up increased only in those patients who experienced clinical benefit. CONCLUSIONS Enhanced external counterpulsation enhances peripheral endothelial function with beneficial effects persisting at one-month follow-up in patients with a positive clinical response. This suggests that improvement in endothelial function may contribute to the clinical benefit of EECP in patients with symptomatic CAD.


This study was undertaken to determine whether enhanced external counterpulsation is a safe and effective treatment for angina in octogenarians. In this prospective observational study, demographic and
clinical outcome data on patients consecutively enrolled in the International EECP Patient Registry was examined. Of the 3037 patients analyzed, 249 (8%) were \( \geq 80 \) years old. Octogenarians were more likely to be female and have a history of congestive heart failure (41% vs. 29%; \( p<0.001 \)). They were less likely to have had previous revascularization. Fewer patients in the octogenarian group (76% vs. 84%; \( p<0.01 \)) completed a course of treatment. Of those octogenarian patients who completed treatment, 76% reported a reduction in angina and quality of life improved significantly. Adverse events related to treatment were low. At 6-month follow-up, 81% reported maintenance of angina improvement. Thus, enhanced external counterpulsation is a low-risk intervention that offers octogenarians the ability to return to more normal activity and a better quality of life.


Enhanced external counterpulsation is a noninvasive technique designed to increase myocardial perfusion and reduce cardiac workload in patients with coronary artery disease. Recent trials have documented beneficial hemodynamic effects. Stress testing and radionuclide imaging have demonstrated improvements in functional capacity and myocardial perfusion. This procedure may be the therapeutic choice for patients with severe diffuse disease or in whom repeat revascularization is not possible. The relatively low cost of the technique makes it feasible for patients in developing countries.

2002


Angina remains a significant health problem in the United States and the world. Although there are a variety of pharmacologic and interventional therapies to treat angina, many patients are not adequately helped by these treatments. Enhanced external counterpulsation (EECP) is an effective, noninvasive technique designed to decrease the frequency and duration of anginal episodes, as well as increase exercise duration in patients with acute angina. Since the early 1960s, the technology of EECP has been thoroughly refined. In addition, a number of important clinical trials have provided evidence for its effectiveness. Continuing research is needed to determine the best patients for EECP and its appropriate clinical application.


A variety of clinical trials of enhanced external counterpulsation (EECP) have been conducted since the 1960s. The vast majority of these studies have investigated the use of EECP in patients with angina pectoris. Only one of these trials was randomized. These clinical trials have demonstrated the benefits of EECP in terms of reduction in anginal episodes, increased exercise times, and improvement in health-related quality of life scores. The International EECP Patient Registry, through its phase I and II enrollment, is expanding the data set on outcomes after EECP treatment.


The mechanisms accounting for the salutary benefits of enhanced external counterpulsation (EECP) remain largely unknown. Emerging data now point to three possible hypotheses to explain its efficacy. These possible explanations include enhanced diastolic flow, changes in the neurohumoral milieu, and changes in ventricular function independent of changes in cardiac load. While each of these three hypotheses may help explain the mechanism behind EECP’s effects, more clinical studies are required to refine these proposed explanations.

Most patients who receive enhanced external counterpulsation (EECP) have symptomatic coronary artery disease. These patients have either responded poorly to pharmacologic therapy or are poor candidates for revascularization procedures. Such patients receive a variety of consistent benefits from EECP treatment. As more is learned about EECP, patients once excluded from early clinical trials are now able to take advantage of EECP. Nevertheless, EECP is not suitable for some patients. It has a favorable adverse event profile for most patients undergoing the treatment. Medicare reimbursement coverage limitations remain an obstacle to having a broad cross-section of patients benefit from EECP.


Patients with coronary artery disease have a variety of treatment options available to them. These include medications to control anginal episodes and, when appropriate, revascularization interventions in the form of coronary artery bypass graft and angioplasty. Despite advances in the treatment of angina, a substantial number of patients continue to have symptoms that can significantly impair their quality of life. These patients may benefit from enhanced external counterpulsation (EECP). With recent results of the latest clinical trial of EECP just published, the role of EECP, including its position in the hierarchy of treatment options, needs to be seriously considered.


There is strong, continued interest in enhanced external counterpulsation (EECP) as evidenced by current, ongoing clinical trials. Many of these have been designed to support the current indications of EECP, mainly its application in the treatment of symptomatic coronary artery disease. An exciting area in this regard is how EECP may help control blood glucose in patients with angina and diabetes mellitus. A variety of planned or ongoing exploratory studies are also helping to explain the mechanism of action behind EECP. Two clinical trials are now investigating a new indication for EECP in patients with congestive heart failure, including the important randomized Prospective Evaluation of EECP in Congestive Heart failure (PEECH) trial.


EECP is a non-invasive outpatient treatment for cardiovascular disease refractory to medical and/or surgical therapy. It has been cleared by the Food and Drug Administration for the treatment of a variety of cardiac conditions including congestive heart failure and chronic stable angina. A course of therapy consists of 35 one-hour treatments given once or twice daily. Augmented diastolic pressure and retrograde flow improve myocardial perfusion, while systolic unloading reduces cardiac workload and oxygen requirements. As a result of this treatment, most patients experience increased time to onset of ischemia, increased exercise tolerance, a reduction in the number and severity of anginal episodes, and improved quality of life. Evidence has been presented that this effect lasts well beyond the immediate post-treatment period with some patients symptom-free for several years. Because patients principally seek medical care to live longer or feel better, heart programs need to offer their patients the latest medical advances which have the potential of improving patient survival and health status (symptoms, functioning, and quality of life). Heart programs face a challenging economic future. Increased competition makes it necessary to implement strategies for market differentiation. Those programs most attuned to what their patients define as critical to quality would be most likely to succeed. Over the past decade, there have been a growing number of patients with chronic angina who have exhausted the standard revascularization armamentarium. Because coronary artery bypass grafts occlude and restenosis occurs at angioplasty sites, many patients no longer have suitable coronary anatomy for additional procedures. Also, as the population ages, the proportion of patients with diffuse coronary disease, congestive heart failure, significant co-morbid illness, and poor functional status increases. The incapacitating effects of angina on patients’ abilities to work, maintain regular social interactions, and
participate in the usual activities of daily living are well described. In spite of the ongoing successes of
catheter-based revascularization techniques, the population of patients with intractable angina continues
to grow; and ironically, advancements in medical therapy have resulted in an increasing number of
patients who are living with severe left ventricular dysfunction and congestive heart failure. Recent
studies have estimated that approximately 5-15% of patients undergoing coronary angiography may be
considered to have advanced coronary artery disease. Considering that 1,713,000 cardiac
catheterizations were performed in 1996 in the United States, approximately 100,000-250,000 patients
per year may be eligible for newer treatments for coronary artery disease. More recent statistics in the
AHA Heart and Stroke Update report that in 2001, nearly one million patients had coronary artery bypass
graft surgery or percutaneous coronary intervention. Of these, 125,650 patients experienced persistent
angina.

- Soran O, Kennard ED, Kelsey SF, et al. Enhanced External Counterpulsation as Treatment
  for Chronic Angina in Patients with Left Ventricular Dysfunction: A Report from the
  International EECP Patient Registry (IEPR). Congestive Heart Failure; 2002
  Nov-Dec;8(6):297-302.

The International Enhanced External Counterpulsation (EECP) Patient Registry tracks acute and long-
term outcome for consecutive patients treated for chronic angina. Although EECP has previously been
shown to be a safe and effective treatment for angina, little information is available on its use in patients
with left ventricular (LV) dysfunction. This report compares the acute outcome and 6-month follow-up for a
group of patients with severe LV dysfunction and a group of patients without LV dysfunction. Of 1,402
patients in the registry recruited in 1998-1999 who had recorded values of LV ejection fraction (LVEF) at
baseline, 1,090 (77.7%) had preserved LV function (LVEF >35%) and 312 (22.3%) had LV dysfunction
(LVEF <=35%). Six-month follow-up was available on 84% of these patients. Pre-EECP patients with LV
dysfunction had a longer history of coronary artery disease (12.9 years vs. 9.1 years; p<0.001), a higher
rate of congestive heart failure (60.6% vs. 20.1%; p<0.001) and myocardial infarction (83.5% vs. 61.9%;
p<0.001). Patients with LV dysfunction had more severe pre-EECP angina, with 86.2% presenting with
Canadian Cardiovascular Society Class III/IV vs. 73.6%; p<0.01. Patients with LV dysfunction, consistent
with their more severe baseline profile, suffered more adverse events (death, unstable angina, and
exacerbation of heart failure) during the treatment period and were less likely to complete the full course.
Immediately post-EECP, angina decreased by at least one class in 67.8% of patients with LV dysfunction
(vs. 76.2%; p<0.01), and 35.9% of LV dysfunction patients vs. 39.0% had discontinued nitroglycerin use
(p=ns). At 6-month follow-up, patients with LV dysfunction showed higher rates of death (9.3% vs. 2.2%;
p<0.001) and exacerbation of congestive heart failure (9.9% vs. 3.7%; p<0.001). Rates of the composite
outcome of death/myocardial infarction/coronary artery bypass grafting/percutaneous coronary
intervention (15.4% vs. 8.3%; p<0.001) were also higher for patients with LV dysfunction. However,
patients not reporting such an event showed maintenance of their improved anginal status, with 81% of
LV dysfunction vs. 83.8% of patients without LV dysfunction (p=ns) reporting angina at 6 months equal to
or less severe than immediately post-EECP, and nitroglycerin use was still reduced at 46.1% for LV
dysfunction vs. 37.4% (p<0.05). The rate of event-free angina maintenance at 6 months was 67.0% for
patients with LV dysfunction and 70.6% of patients with preserved LV function (p=ns). Patients with LV
dysfunction achieved a less robust reduction in angina than did those without LV dysfunction. For the
majority of the patients in the registry, this reduction was maintained at 6 months.

- Michaels AD, Accad M, Ports TA, Grossman W. Left Ventricular Systolic Unloading and
  Augmentation of Intracoronary Pressure and Doppler Flow During Enhanced External

BACKGROUND Enhanced external counterpulsation (EECP) is a noninvasive, pneumatic technique that
provides beneficial effects for patients with chronic, symptomatic angina pectoris. However, the
physiological effects of EECP have not been studied directly. We examined intracoronary and left
ventricular hemodynamics in the cardiac catheterization laboratory during EECP. METHODS AND
RESULTS Ten patients referred for diagnostic evaluation underwent left heart catheterization and
coronary angiography from the radial artery. At baseline and then during EECP, central aortic pressure,
intracoronary pressure, and intracoronary Doppler flow velocity were measured using a coronary
catheter, a sensor-tipped high-fidelity pressure guidewire, and a Doppler flow guidewire, respectively. Similar to changes in aortic pressure, EECP resulted in a dramatic increase in diastolic (71±10 mm Hg at baseline to 137±21 mm Hg during EECP; +93%; P<0.0001) and mean intracoronary pressures (88±9 to 102±16 mm Hg; +16%; P=0.006) with a decrease in systolic pressure (116±20 to 99±26 mm Hg; -15%; P=0.002). The intracoronary Doppler measure of average peak velocity increased from 11±5 cm/s at baseline to 23±5 cm/s during EECP (+109%; P=0.001). The TIMI frame count, a quantitative angiographic measure of coronary flow, showed a 28% increase in coronary flow during EECP compared with baseline (P=0.001). CONCLUSIONS EECP unequivocally and significantly increases diastolic and mean pressures and reduces systolic pressure in the central aorta and the coronary artery. Coronary artery flow, determined by both Doppler and angiographic techniques, is increased during EECP. The combined effects of systolic unloading and increased coronary perfusion pressure provide evidence that EECP may serve as a potential mechanical assist device.


Enhanced external counterpulsation is a non-invasive cardiac assist procedure that has been shown to significantly reduce the symptoms of recurring chest pain, shortness of breath and fatigue experienced by patients with moderate to severe angina pectoris as the result of coronary artery disease. EECP® treatment, which has been in wide use for more than a decade, has proven to be a highly effective and safe alternative for patients who are not appropriate candidates for the traditional revascularization procedures of coronary angioplasty or bypass graft (CABG) surgery. The recent 2002 annual meeting of the American College of Cardiology featured a comprehensive session on the clinical experience gained with use of external counterpulsation, presented by leading authorities in cardiovascular medicine from major university teaching center across the country. More extensive clinical investigations are currently underway, examining the potential role of EECP® therapy in treating such imminently life-threatening conditions as congestive heart failure. Based on clinical results achieved to date, EECP® therapy should be considered a significant component of the available armamentarium for the treatment of patients with coronary artery disease and its associated symptoms.


To assess the feasibility of using enhanced external counterpulsation to treat patients with heart failure, 26 patients with stable heart failure (New York Heart Association classes II-III), with a left ventricular ejection fraction at or below 35%, and without fluid overload, were treated with enhanced external counterpulsation (1 hour daily, 5 days a week, to a total of 35 hours). Patients were followed for 6 months after completing the course of enhanced external counterpulsation. The primary parameter was safety as reflected by adverse events or by changes in laboratory parameters. Secondary end points included changes in exercise capacity and quality of life. There were no clinically significant problems associated with the administration of enhanced external counterpulsation. Significant improvements were seen in exercise capacity (peak oxygen uptake and exercise duration), and in quality of life assessments, at 1 week and 6 months after the course of enhanced external counterpulsation. This study suggests that enhanced external counterpulsation is safe and well tolerated in patients with stable heart failure, and that a randomized, controlled study of enhanced external counterpulsation in these patients is warranted.


Among 2,486 patients enrolled in the International EECP Patient Registry (IEPR) who underwent EECP therapy for symptomatic coronary artery disease, the median diastolic augmentation (DA) ratio increased from 0.7 to 1.0 from the beginning to the end of treatment. Patients who had the greatest increase in the DA ratio had the greatest reduction in angina class, whereas those with a relative decrease in the DA
ratio had the lowest reduction in angina class immediately after EECP and at 6 months of follow-up. These data suggest that improved vascular tone during EECP treatment may play a mechanistic role in the relation between DA and clinical benefit with EECP.


Enhanced external counterpulsation (EECP) has recently emerged as a treatment option for angina in selected patients suitable for revascularization with percutaneous coronary intervention (PCI). We compared baseline characteristics and 1-year outcome in 2 cohorts of PCI candidates presenting with stable symptoms: 323 patients treated with EECP in the International EECP Patient Registry (IEPR), and 448 NHLBI Dynamic Registry patients treated with elective PCI. Compared with patients receiving PCI, IEPR patients had a higher prevalence of many risk factors including prior PCI (53.0% vs 33.3%, p <0.001), prior coronary artery bypass grafting (42.1% vs 18.6%, p <0.001), prior myocardial infarction (56.4% vs 27.8%, p <0.001), history of congestive heart failure (16.8% vs 9.2%, p <0.01), and history of diabetes (37.9% vs 23.5%, p <0.001). Left ventricular ejection fraction was lower among IEPR patients (mean 50.3% vs 59.2%, p <0.001). At 1 year, survival was comparable in the 2 cohorts (98.7% IEPR vs 96.8% PCI, p = NS), as were rates of coronary artery bypass grafting during follow-up (4.5% IEPR vs 5.7% PCI, p = NS). At 1 year, 43.7% of IEPR patients reported no anginal symptoms compared with 73.4% of Dynamic Registry patients (p <0.001). Rates of severe symptoms (Canadian Cardiovascular Society class III, IV, or unstable) at 1 year were 15.5% among IEPR patients and 9.5% in the Dynamic Registry (p = 0.02). PCI candidates suitable for and treated with EECP had 1-year major event rates comparable to patients receiving elective PCI. Although PCI was associated with substantially lower rates of 1-year symptoms, EECP may be a safe treatment option for selected patients with obstructive coronary disease.


Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for patients with coronary artery disease (CAD). EECP has been demonstrated to improve aninal class and time to ST-segment depression during exercise stress testing. This study assesses the efficacy of EECP in improving stress-induced myocardial ischemia using radionuclide perfusion treadmill stress tests (RPSTs). The international study group enrolled patients from 7 centers with chronic stable angina pectoris and a baseline ischemic pre-EECP RPST. Patients’ demographic and clinical characteristics were recorded. A baseline pre-EECP maximal RPST was performed within 1 month before EECP treatment. The results were compared with a follow-up RPST performed within 6 months of completion of a 35-hour course of EECP. Four centers performed post-EECP RPST to the same level of exercise as pre-EECP, whereas 3 centers performed maximal RPST post-EECP. The study enrolled 175 patients (155 men and 20 women). Improvement in angina, defined by > or =1 Canadian Cardiovascular Society angina class change, was reported in 85% of patients. In the centers performing the same level of exercise, 81 of 97 patients (83%) had significant improvement in RPST perfusion images. Patients who underwent maximal RPST revealed improvement in exercise duration (6.61 ± 1.88 pre-EECP vs 7.41 ± 2.03 minutes post-EECP, p <0.0001); 42 of the 78 patients (54%) in this group showed significant improvement in RPST perfusion images. Thus, EECP was effective in improving stress myocardial perfusion in patients with chronic stable angina at both comparable (baseline) and at maximal exercise levels.

BACKGROUND The Multicenter Study of Enhanced External Counterpulsation (MUST-EECP) was the first prospective, randomized, blinded, sham-controlled study of enhanced external counterpulsation (EECP) in the treatment of chronic stable angina. We previously reported that EECP therapy lengthens the time to exercise-induced myocardial ischemia and reduces angina. We now describe the effects of EECP therapy versus a sham-treated control group in terms of patients’ functioning, their senses of well-being and other Health-Related Quality Of Life (HQOL) parameters from baseline to end of treatment and from baseline to 12 months after treatment. OBJECTIVE To determine whether a 35-hour course of EECP affects the HQOL of patients with symptomatic coronary artery disease, 12 months following treatment. METHODS Seventy-one of the 139 patients enrolled in MUST-EECP provided evaluable patient-completed questionnaires at baseline, at the end of treatment, and 12 months post-treatment. The Medical Outcomes Study 36-Item Short-Form Health Survey and the Quality of Life Index-Cardiac Version III were used to assess effects on HQOL. RESULTS Both groups had similar HQOL scores at baseline. At end of treatment and at 12-month follow up, patients who had active-CP reported greater improvement than those who had inactive-CP in all nine quality of life scales, including ability to perform activities of daily living, ability to work, bodily pain, confidence in health, energy, ability to engage in social activities with family and friends, anxiety and depression, and quality of life issues from the effects of angina on health and functioning. Despite small sample sizes, active-CP patients demonstrated significantly greater improvement at 12 months following treatment in bodily pain, social functioning, and quality of life specific to cardiac patients compared with inactive-CP patients. CONCLUSION Significant health-related quality of life improvements were measurable up to 12 months after the completion of treatment with EECP. Improvements in this controlled study are consistent with HQOL changes reported in case series and patient registries. Larger studies are warranted.

2001


BACKGROUND Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for patients with angina pectoris. However, the hemodynamic effects of EECP are still unknown and have been theorized to simulate the clinical use of the intra-aortic balloon pump, enhancing cardiac output, stroke volume, and retrograde aortic diastolic flow. METHODS Twelve hemodynamic parameters were measured, using the BioZ System (CardioDynamics International Corporation, San Diego, Calif) after 1 hour (n=22) and after 35 hours (n=16) of EECP treatment compared with baseline. The BioZ System noninvasively measures hemodynamic parameters using the thoracic electrical bioimpedance method. RESULTS One hour of EECP treatment revealed a significant decrease in cardiac output, stroke volume, contractility, afterload, preload, and myocardial energy production, but systolic time ratios and thoracic fluid content were unchanged. However, after 35 hours of therapy, stroke volume (P < or = 0.05), index of contractility (P < or = 0.05), and thoracic fluid content (P < or = 0.01) were decreased. CONCLUSIONS The acute reduction in contractility, preload, and concurrent bradycardia may have favorable hemodynamic effects for patients with angina pectoris. Further studies are needed to elucidate the mechanism of EECP therapy and its efficacy for patients with angina pectoris.


Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for coronary artery disease. The mechanism of action is felt to be hemodynamic. The complex hemodynamic effects have been simply quantified by calculating a previously described effectiveness ratio (ER). The EECP Clinical Consortium, a clinical registry of 37 centers, prospectively enrolled 395 chronic stable angina patients (79 women, 316 men, mean age 66 years) to examine the relation of the ER to posttreatment improvement in Canadian Cardiovascular Society angina class (CCS). Women and the elderly underwent planned subgroup analysis. The ER was calculated during the first and last hours of a 35-hour course of EECP treatment. After EECP, CCS improved by at least 1 class in 88% of patients, 87% of men and 92% of...
women (p = NS), and in 89% of patients < or = 66 years and 88% of patients > 66 years old (p = NS). The initial and final ER were similar in patients with and without improvement in CCS. Significant first-hour ER differences were seen between men and women (0.96 +/- 0.03 vs 0.76 +/- 0.04, p<0.005), and between ages < or = 66 and > 66 years old (1.04 +/- 0.04 vs 0.81 +/- 0.03, p<0.0001). However, all subgroups responded equally well to EECP treatment. EECP is effective in improving CCS in chronic stable angina patients; it has comparable effects in men and women and across a broad range of ages. The hemodynamic effect of EECP (ER) does not predict improvement in CCS and may indicate that other factors, such as neurohormonal changes, may have a significant role in mediating the observed EECP benefits.


Since 1998 the International Enhanced External Counterpulsation Patient Registry (IEPR) has collected data on baseline characteristics, safety and acute and long-term outcome of consecutively enrolled patients undergoing EECP for chronic angina. The majority of patients receiving EECP have severe angina, have had previous revascularization, and are no longer suitable for either bypass surgery or percutaneous intervention. Patients show a high rate of comorbid conditions such as diabetes, and congestive heart failure. After a mean treatment time of 34 hours, 72% of patients showed reduction in angina. Major adverse coronary events during treatment period are infrequent. On a sample of patients followed to one year, the majority maintain their reduction in angina without occurrence of any major coronary event.


Enhanced external counterpulsation (EECP) is used to noninvasively treat refractory angina patients, including those with a history of heart failure. The International EECP Patient Registry was used to examine the benefit and safety of EECP treatment, including a 6-month follow-up, in 1,957 patients, 548 with a history of heart failure. The heart failure cohort was older, with more females, a greater duration of coronary artery disease, more prior infarcts and revascularizations. Significantly fewer heart failure patients completed the course of EECP, and exacerbation of heart failure was more frequent, though overall major adverse cardiac events (MACE, i.e. death, myocardial infarction, revascularization) during treatment were not significantly different. The angina class improved in 68%, with comparable quality of life benefit, in the heart failure cohort. At 6 months, patients with congestive heart failure maintained their reduction in angina but were significantly more likely to have experienced a MACE end point.


Background External counterpulsation (ECP) is a new noninvasive means of augmenting organ perfusion by applying ECG triggered diastolic pressure to the vascular bed of the lower limbs. In this study, effects of ECP on changes of ocular blood flow velocities were studied. Method Mean, systolic and diastolic flow velocities of the ophthalmic artery were measured by Doppler sonography before and during ECP. Twelve healthy volunteers (age 31.3±4.3 years) and 12 patients with severe atherosclerosis (inclusion criteria: two atherosclerotic risk factors, at least one severe coronary stenosis, age 62.1±5.3 years) were included in the study. Results In healthy subjects, ECP changed diastolic flow velocity of the ophthalmic artery non-significantly from 21.6±7.7 to 23.7±10.8 cm/s. Systolic flow velocity decreased significantly from 36.1±13.6 to 28.9±10.2 cm/s (p<0.01). Mean flow velocity changed non-significantly from 28.1±9.4 to 26.5±9.9 cm/s. In atherosclerotic patients, mean flow velocity increased significantly from 26.3±11.4 to 29.3±11.2 cm/s (p<0.01), which was caused by significant diastolic flow augmentation from 19.7±9.1 to
23.9±9.7 cm/s (p<0.01). Systolic flow velocity was not changed significantly (from 34.2±12.8 to 32.6±11.8 cm/s). Conclusion No significant change of mean blood flow velocity in the ophthalmic artery was found in young healthy subjects. In elderly patients with atherosclerosis, ECP significantly increased blood flow velocity in the ophthalmic artery by 11.4%. This may indicate an ocular perfusion benefit in these patients as a result of ECP and could also explain the increase of perfusion found in patients with retinal ischemia after ECP.


AIMS The mechanism by which enhanced external counterpulsation therapy exerts its beneficial effects on chronic and symptomatic stable angina is largely unknown. To clarify the mechanism of action of enhanced external counterpulsation, we used(13)N-ammonia positron emission tomography to evaluate myocardial perfusion. METHODS AND RESULTS This was not a randomized controlled study. Eleven patients (eight male, age: 61.6+/-9.7) with angina pectoris underwent enhanced external counterpulsation therapy for 35 1 h sessions. They underwent a treadmill exercise test and(13)N-ammonia positron emission tomography, both at rest and with dipyridamole, before and after enhanced external counterpulsation therapy. Neurohumoral factors and nitric oxide were also evaluated. Myocardial perfusion increased at rest after therapy (0.69+/-0.27 to 0.85+/-0.47 ml x min(-1) x g(-1), P<0.05). In ischaemic regions, particularly the anterior region, myocardial perfusion at rest and with dipyridamole and coronary flow reserve improved significantly after therapy (at rest: 0.71+/-0.26 to 0.86+/-0.31;P<0.05, with dipyridamole: 1.26+/-0.65 to 1.84+/-0.94;P<0.02, coronary flow reserve: 1.75+/-0.24 to 2.08+/-0.28;P<0.04). Exercise time was prolonged and the time to 1-mm ST depression improved markedly (P<0.01). After therapy, nitric oxide levels increased (P<0.02) and neurohumoral factors decreased.

CONCLUSIONS Enhanced external counterpulsation therapy improved myocardial perfusion at rest and with dipyridamole and was associated with an increased exercise tolerance with(13)N-ammonia positron emission tomography and increased nitric oxide levels. These results suggest that one of the enhanced external counterpulsation mechanisms is development and recruitment of collateral vessels.


Clinical restenosis following coronary artery angioplasty (PTCA) occurs in up to 30% of the patients within 6 months of treatment. Endothelial dysfunction in diseased and/or mechanically injured arteries may be a key factor in the process. Enhanced External Counterpulsation (EECP) is an effective noninvasive treatment for coronary artery disease (CAD), which has recently been shown to augment nitric oxide (NO) production. Thus, we postulate that EECP would reduce the restenosis rates after PTCA through its effects on endothelial function. 24 patients (pts) one-month post successful PTCA were randomized to EECP (15 pts) or Control (9 pts). At 6 month follow-up MACE and recurrence of ischemia in the PTCA related regions demonstrated by scintigraphy were observed in 13% of the EECP treated group and in 44% of the Control group (p<0.01). This pilot study suggests that further investigation of EECP in reducing restenosis is warranted.

The effects of enhanced external counterpulsation (EECP) on Renin-Angiotensin System (RAS) activity in acute MI (AMI) were studied in 18 dogs divided into three groups: Control (N=6), AMI (N=6) and AMI+EECP (N=6). The LAD in AMI groups was occluded, with EECP performed 60-180 minutes post occlusion in the AMI+EECP group. Plasma renin activity, angiotensin II, angiotensin converting enzyme were measured at baseline, 60, 120, and 180 minutes. Baseline values were similar. AMI significantly increased RAS activity and this activity increased with occlusion time. However, EECP reversed RAS changes towards control values. EECP decreases in RAS activity may be mediated by hemodynamic effects and shear stress induced increase in nitric oxide, and may potentially alter cardiovascular remodeling post AMI.


Patient characteristics, including demographics, cardiac history and function, medical treatment of 2,899 patients from the International EECP Patient Registry (IEPR) were used to determine patient characteristics in predicting unfavorable events. Diabetes mellitus and multivessel coronary artery disease (CAD) were potent predictors of MACE (death, MI, CABG, PCI) during the course of EECP treatment. In the present group of high risk, largely unrevascularizable patients treated with EECP, the overall risk of MACE was low, even in the diabetic and multivessel CAD groups.


Background In 1998, the International EECP Patient Registry (IEPR) was organized to document patient characteristics, safety, and efficacy during the treatment period, and long-term outcomes. All centers with EECP facilities were invited to join the voluntary Registry. The Registry population comprises all patients starting EECP therapy for treatment of angina pectoris in participating centers. Hypothesis The study was undertaken to determine whether EECP is a safe and effective treatment for patients with angina pectoris regardless of their suitability for revascularization by more conventional techniques. Methods After 18 months of operation, 43 clinical centers representing over half of clinical sites using the EECP system contributed cases. The data reported here were collected before the first EECP treatment and upon completion of final treatment. EECP can be used for patients ineligible for either coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI), as well as for those who prefer noninvasive treatment to avoid or delay revascularization. In this report, patients considered to be candidates for revascularization are compared with those not considered suitable. Results Of the 978 patients analyzed, 70% had Canadian Cardiovascular Society Classification class III or IV angina before starting treatment, and 62% used nitroglycerin. Most (81%) had been previously revascularized, and 69% were considered unsuited for either PCI or CABG at the time of starting EECP. A full treatment course (usually 35 h) was completed in 86%, of whom 81% reported improvement of at least one angina class immediately after the last treatment. Conclusion In a broad patient population, EECP has been shown to be a safe and effective treatment.


BACKGROUND Enhanced external counterpulsation (EECP) has been demonstrated to be an effective treatment for stable angina in patients with coronary disease. The hemodynamic effects of EECP are maximized when the ratio of diastolic to systolic pressure area is in the range of 1.5 to 2.0. HYPOTHESIS It is hypothesized that patients undergoing EECP who are able to achieve higher diastolic augmentation (DA) ratios may derive greater clinical benefit. This study examines the relationship between the DA ratio.
and clinical outcomes in patients undergoing EECP. METHODS We analyzed demographic, noninvasive hemodynamic, and clinical outcome data on 1,004 patients enrolled in the International EECP Patient Registry (IEPR) for treatment of chronic angina between January 1998 and August 1999. Blood pressure waveforms were recorded from finger plethysmography. Six-month clinical outcomes were obtained by telephone interview. RESULTS At the end of EECP treatment, 370 (37%) patients had a higher DA ratio (defined as $>$ or $= 1.5$) and 634 (63%) had a lower DA ratio (defined as $< 1.5$). Factors associated with a lower DA ratio included age $>$ or $= 65$ years ($p < 0.001$), female gender ($p < 0.001$), left ventricular ejection fraction $< 35\%$ ($p < 0.05$), hypertension ($p < 0.01$), prior coronary bypass surgery ($p < 0.01$), noncardiac vascular disease ($p < 0.001$), multivessel disease ($p < 0.01$), congestive heart failure ($p < 0.01$), current smoking ($p < 0.01$), unsuitability for further revascularization ($p < 0.001$), and higher baseline angina class ($p < 0.001$). There were no significant differences regarding diabetes mellitus, prior coronary angioplasty, prior myocardial infarction, or antianginal medication use between patients with higher or lower DA ratios. Based on a multiple logistic regression model, independent predictors of a DA ratio $< 1.5$ at the end of EECP included current smoking (odds ratio 3.3; 95% confidence intervals 2.0-5.4); multivessel disease (1.7; 1.3-2.3); female gender (2.2; 1.7-3.0); no prior EECP (1.9; 1.1-3.3); noncardiac vascular disease (2.3; 1.7-2.9); age $>$ or $= 65$ years (1.7; 1.4-2.2), and patients not suitable for revascularization (1.6; 1.2-2.0). By the end of therapy, there were no significant differences in myocardial infarction, revascularization rates, or nitroglycerin use with respect to higher DA ratios. At 6-month follow-up, patients with higher DA had a trend toward a greater reduction in angina class compared with those with lower DA ($p = 0.069$). There was a significantly higher rate of unstable angina and congestive heart failure in the group not achieving higher augmentation ($p < 0.05$). CONCLUSIONS Patients who are younger, male, nonsmoking, and without multivessel coronary or noncardiac vascular disease are most likely to have higher DA with EECP. Patients with higher DA tended to have a greater reduction in angina class at 6-month follow-up compared with those with lower DA ratios. There is evidence that higher DA ratios are associated with improved short


Enhanced external counterpulsation (EECP) is a noninvasive, counterpulsative method to provide temporary aid to the failing heart by sequentially inflating cuffs on the lower extremity out-of-phase with the left ventricle. Optimization of the method necessitates consideration of the hemodynamics created by EECP and the mode of action providing patient benefit. A computational model based on the governing one-dimensional equations is developed that simulates cardiovascular hemodynamics during EECP. The model includes a 30-element arterial system including the left ventricle, bifurcations, and peripheral arterial vessels. Effects of vessel collapse as external pressure is applied, arterial refilling on pressure release, changes in aortic pressure, and shear stress generated in the arteries are each investigated. Device parameters are systematically varied to determine their effect on system performance. Results show the potential for significant collapse and shear augmentation throughout the arteries of the lower extremity. Performance is strongly influenced by the mean level of external pressurization and the timing of cuff inflation, but less so by the relative timing and pressure differences between cuff segments.


Enhanced external counterpulsation (EECP) is a noninvasive technique that has shown promise in the treatment of ischemic coronary artery disease. Patients undergoing EECP were tested for alterations in psychosocial state associated with treatment. Overall perception of health and quality of life improved with EECP. There was also significant improvement in levels of depression, anxiety, and somatization but no change in levels of anger or hostility. On most measures, change was more significant for subjects who showed objective evidence of resolution of ischemia. Given the known predictive relationship between depression and mortality from cardiac disease, the improvement in depression scores through EECP indicates a finding of potential importance that may warrant further study in future research.

Enhanced external counterpulsation (EECP) is a noninvasive outpatient therapy for the treatment of chronic angina. EECP treatment produces an acute hemodynamic effect that is similar to that produced by the invasive intra-aortic balloon pump. Three sets of cuffs on the upper thigh, lower thigh, and calves of each leg are inflated with compressed air during the diastolic phase of the cardiac cycle and are deflated in early systole. This rapid inflation and deflation raises diastolic aortic pressure, increases coronary perfusion pressure, and provides improved afterload reduction and increased venous return with a subsequent increase in cardiac output. Enhanced external counterpulsation has been shown to provide long-term symptom relief in patients with ischemic heart disease in several case series, as well as in a randomized trial. Up to 80% of patients selected for treatment have a positive clinical response, and an associated objective improvement has been demonstrated by functional imaging in several case series. A treatment course consists of 35 1-hour sessions over a 7-week period and is generally well tolerated with a low risk of adverse events. Development and enhancement of collateral channels, as well as peripheral conditioning and neurohumoral effects, may play a role in providing symptomatic relief. Studies are ongoing to determine the mechanism of action and to further define subsets of patients who might benefit.


**OBJECTIVES** We examined whether enhanced external counterpulsation (EECP) improves myocardial ischemia, exercise tolerance and cardiac function in patients with coronary artery disease (CAD). **BACKGROUND** Enhanced external counterpulsation reduces angina and improves exercise tolerance in patients with CAD. Some objective improvements of ischemia by EECP have been reported, but they should be confirmed further. Detailed hemodynamic effects of EECP have been less well documented. **METHODS** Enhanced external counterpulsation was performed for a total of 35 h in patients with stable CAD (n = 12) who showed evidence of exercise-induced myocardial ischemia despite conventional medical or surgical therapies. All patients had significant stenotic lesions in major coronary arteries. **RESULTS** Enhanced external counterpulsation improved all exercise test parameters (p < 0.05): exercise duration, time to 1-mm ST segment depression, rate-pressure product at peak exercise and rate-pressure product at 1-mm ST segment depression. Moreover, the prevalence of exercise-induced reversible perfusion defects by thallium scintigraphy decreased after treatment (p < 0.01). Enhanced external counterpulsation did not alter systolic function but improved diastolic filling, left ventricular (LV) end-diastolic pressure (p < 0.05) by cardiac catheterization and LV peak filling rate end-diastolic volume/s (p < 0.01) and time to peak filling rate (p < 0.05) by radionuclide scintigraphy. These hemodynamic improvements were associated with decreased plasma brain natriuretic peptides levels after EECP (p < 0.05). **CONCLUSIONS** Thus, EECP treatment improves exercise tolerance and reduced myocardial ischemia by thallium scintigraphy in association with improved LV diastolic filling in patients with stable CAD.

2000


Enhanced external counterpulsation (EECP) produces sequenced compression of the lower extremities during diastole. The "milking" effect on the arterial beds of the lower extremities augments aortic diastolic pressure and thereby increases coronary perfusion pressure and blood flow. The simultaneous compression of venous beds increases venous return and cardiac filling pressure. EECP treatment of patients with chronic angina can improve myocardial perfusion as demonstrated by radionuclide stress imaging, time to significant ST-segment depression during exercise testing, and functional status. EECP may be especially worth considering for patients with severe, diffuse coronary artery disease in whom
targets for surgical revascularization are lacking and those who have persistent angina after 1 or more revascularization procedures.

- **Lawson WE, Hui JCK, Lang G.** Treatment benefit in the enhanced external counterpulsation consortium. *Cardiology.* 2000; 94:31-35

Patient Population 2289 consecutive patients with angina pectoris, CCS functional Classes I-IV, who have EECP at 84 participating centers (university medical centers, hospitals, clinics, physician’s offices and rehabilitation facilities) were included in this study. Treatment protocol Patients were treated with daily 1- to 2-hour EECP sessions 5 days a week to a total of 35 hours. Measurement: Classification of angina before and after EECP, intervening major adverse cardiovascular events, other adverse events. Results 74% of CCS Class II-IV patients improved their functional class; 39.5% of Class III-IV patients improved 2 or more classes. There was a low incidence of morbidity (4%, mostly related to skin and musculoskeletal trauma). Safety and efficacy across a broad population with angina is demonstrated.


Nearly 8 million people in the United States suffer from symptoms of coronary artery disease (CAD). Unfortunately, the population of patients with ischemic coronary disease that is not readily amenable to surgical or percutaneous revascularization continues to grow. For patients who are not candidates for standard revascularization procedures and in whom aggressive medical therapy fails to control symptoms, enhanced external counterpulsation (EECP) is a new, noninvasive outpatient method to improve quality of life by decreasing ischemic symptoms and permit increased activity. We report the case of a 56-yearold woman with severe, symptomatic CAD receiving maximal medical therapy who underwent a course of EECP therapy because she was not a good candidate for other forms of revascularization. She demonstrated dramatic improvement in her anginal symptoms and complete resolution of myocardial ischemia on repeat nuclear stress imaging. This case suggests that EECP is a safe and effective method for reducing symptoms of myocardial ischemia in patients for whom standard percutaneous or surgical revascularization is not suitable treatment.


Patient Population 39 patients with acute myocardial infarction (MI); all patients underwent balloon angioplasty within 12 hours of onset of chest pain and all patients were given heparin while in the coronary care unit. 12 received intra-aortic balloon pumping (IABP), 27 received EECP, 4 did not complete treatment with EECP. Treatment Protocol: Either IABP or EECP for sixty minutes. Measurements Heart rate, right atrial pressure, pulmonary capillary wedge pressure, cardiac index, area under artery pressure tracing in systole, area under artery pressure tracing in diastole, systolic systemic vascular resistance. All parameters were measured at baseline, at 15 minute intervals during treatment, and 60 minutes after the end of treatment. Results No adverse effects, including bleeding from cannulation sites or interference with oxygenation estimated by oximetry were observed. The hemodynamic effects of EECP were similar to those of IABP in diastolic augmentation. However, right atrial pressure, pulmonary capillary wedge pressure, and cardiac index increased during EECP in contrast to IABP. These effects suggest that EECP increases venous return, raises the cardiac preload, and increases cardiac output.

Patient Population A cohort of 33 consecutive patients with CAD and stable, but limiting angina who were treated with EECP between 1989 and 1991 and followed for a mean of 5 years (4-7 years). Patients were divided into 2 groups: those with evidence of improved myocardial perfusion (Responders) and those without (Nonresponders). Treatment Protocol Daily 1- to 2-hour sessions 5 days a week for a total treatment course of 35 hours. Measurements: Radionuclide stress tests pre- and post-EECP, major adverse cardiovascular events (MACE) during follow up. Results 79% of patients demonstrated improved perfusion post-EECP. Overall, 64% were alive and without interim cardiovascular events or need for revascularization at a mean follow-up of 5 years. Death and MACE was significantly lower in Responders (23%) versus Nonresponders (86%).

1999


Patient Population This study was undertaken to evaluate hemodynamics effects after 1-hour of EECP in volunteers. Treatment Protocol: 1-hour of EECP. Measurements Changes in flow volumes in carotid, vertebral, hepatic, renal and internal iliac were measured by duplex sonography, and stroke volume was measured by echocardiography. Results This study showed that EECP leads to significant increase in perfusion of brain, liver, kidneys and myocardium. Increase in flow volume is accompanied by an increase in mean arterial pressure by 15% and a down regulation of vasoconstrictive hormones endothelin and renin by 75 to 80%.


Enhanced external counter pulsation is a noninvasive therapy that uses sequentially inflated pneumatic cuffs on the lower extremities to enhance coronary artery diastolic flow and decrease left ventricular afterload. We studied its effect on 18 patients with persistent angina despite maximal medical, surgical and catheter-based interventions. After enhanced external counter pulsation all subjects improved their functional class. Treatment with enhanced external counter pulsation improved functional class significantly from baseline 3.1 ± 0.6 to 1.6 ± 0.5 (p < .001). These results are consistent with the national experience. Growing physician awareness, recent Medicare approval status, and subsequent reimbursement will hopefully increase the use of this therapy.


This is a case report on a 63-year-old male referred with severe substernal chest discomfort, present at rest with minimal exercise (Canadian Cardiovascular Society grade IV angina). He had sustained three prior myocardial infarctions and underwent two coronary artery bypass grafting procedures. He had a permanent cardiac pacemaker. His medications included aspirin, long-acting nitrates, a calcium-channel blocker and an HMG-CoA reductase inhibitor. He took 10-20 sublingual nitroglycerin tablets daily to relieve his chest discomfort. His physical and laboratory examinations were unremarkable. He completed 35-treatment course of enhanced external counterpulsation (EECP) therapy over a seven-week period. He had no side efforts from the therapy and achieved appropriate level of diastolic to systolic augmentation during treatment. He is now doing well and has very infrequent episodes of angina usually occurring with only maximal exertion (CCS class I angina). Long-acting nitrates have been stopped, and remarkably, he now takes only one to two sublingual nitroglycerin tablets per month. He now walks regularly and enjoys deer hunting, yard work and traveling. On the most recent treadmill exercise stress test he completed five minutes on a Bruce protocol achieving 90% of his age predicted maximal heart rate. He had 1 mm ST-segment depression at peak exercise, and the test was terminated secondary to dyspnea. There was no exercise induced chest discomfort.

In addition to symptomatic relief of symptoms and an increase in angina-free walking time with antianginal drugs or revascularization procedures, the recent emphasis of treatment has been to reduce adverse clinical outcomes (coronary death and myocardial infarction). The role of smoking cessation, aspirin, treatment of elevated lipids, and treatment of high blood pressure in all patients and of beta-blockers and angiotensin-converting enzyme inhibitors in patients with diminished systolic left ventricular systolic function in reducing adverse outcomes has been well established. What is unknown, however, is whether any anti-anginal drugs (beta-blockers, long-acting nitrates, calcium channel blockers) affect adverse outcomes in patients with stable angina pectoris. Recent trials evaluated the usefulness of suppression of ambulatory ischemia in patients with stable angina pectoris, but it remains to be established whether suppression of ambulatory myocardial ischemia with antianginal agents or revascularization therapy is superior to pharmacologic therapy targeting symptom relief. Patients who have refractory angina despite optimal medical treatment and are not candidates for revascularization procedures may be candidates for newer techniques of transmyocardial revascularization, enhanced external counterpulsation, spinal cord stimulation, or sympathectomy. The usefulness of these techniques, however, needs to be confirmed in large randomized clinical trials.


**OBJECTIVES** The purpose of this study was to assess safety and efficacy of enhanced external counterpulsation (EECP). **BACKGROUND** Case series have shown that EECP can improve exercise tolerance, symptoms and myocardial perfusion in stable angina pectoris. **METHODS** A multicenter, prospective, randomized, blinded, controlled trial was conducted in seven university hospitals in 139 outpatients with angina, documented coronary artery disease (CAD) and positive exercise treadmill test. Patients were given 35 h of active counterpulsation (active CP) or inactive counterpulsation (inactive CP) over a four- to seven-week period. Outcome measures were exercise duration and time to $1\text{-mm ST}$-segment depression, average daily anginal attack count and nitroglycerin usage. **RESULTS** Exercise duration increased in both groups, but the between-group difference was not significant (p<0.3). Time to 1-mm ST-segment depression increased significantly from baseline in active CP compared with inactive CP (p<0.01). More active-CP patients saw a decrease and fewer experienced an increase in angina episodes as compared with inactive-CP patients (p<0.05). Nitroglycerin usage decreased in active CP but did not change in the inactive-CP group. The between-group difference was not significant (p>0.7). **CONCLUSIONS** Enhanced external counterpulsation reduces angina and extends time to exercise-induced ischemia in patients with symptomatic CAD. Treatment was relatively well tolerated and free of limiting side effects in most patients.


Enhanced external counterpulsation (EECP) is a noninvasive treatment for chronic stable angina, which works by recruiting and developing the coronary collateral vessels. Coronary perfusion and coronary flow reserve (CFR) were evaluated by nitrogen-13 (13N) ammonia positron emission tomography (PET) in a patient who had undergone EECP. The patient, who had 3-vessel coronary artery disease, required a percutaneous transluminal coronary angioplasty (PTCA) for the right coronary artery. The PTCA was successful, but 6 months later he again felt chest oppression. The coronary angiography showed restenosis at the PTCA site, and other progressive coronary stenosis. The patient was again treated with EECP for 35 h. The 13N-ammonia PET was performed both at baseline and during dipyridamole provocation, before and after EECP treatment. Coronary perfusion of each myocardial wall increased at the baseline (anterior: 0.52–0.75; septal: 0.48–0.66; lateral: 0.61–0.68; inferior: 0.46–0.57 ml min$^{-1}$ g$^{-1}$), and the CFRe$s$ in the septal and inferior walls (septal: 2.07–2.15; inferior: 1.99–2.06) also increased after
the treatment. Thus, the EECP treatment improved both coronary perfusion at baseline and CFR, which suggests that it may be one of the choices for treatment of angina.


Studies over the past several decades support the hypothesis that enhanced external counterpulsation (EECP) can provide long-term benefits in patients with angina secondary to chronic coronary disease. Numerous non-sham controlled trials have recently been substantiated by a multicenter, randomized trial. Although the mechanism by which this mechanical treatment effects an alteration in cellular processes within the myocardium remains unclear, recent scientific investigations suggest that shear stress induced by chronic exposure to EECP might result in the release of a variety of growth factors and the subsequent stimulation of angiogenesis in the coronary beds. Ongoing clinical trials in patients with significant left ventricular dysfunction, an international registry, and additional clinical trials may help to elucidate further the role of this novel and unique therapy in our clinical armamentarium.


This article summarizes current invasive and non-invasive techniques and among them EECP available today to treat patients with residual angina in spite of revascularization and optimal drug treatment and/or in patients in whom revascularization cannot be done.

1998


Enhanced external counterpulsation (EECP) is a noninvasive treatment modality, which can increase arterial blood flow in peripheral and coronary arterial disease. Several studies have demonstrated an increase in the flow of the internal iliacal artery and in carotid and renal perfusion during EECP treatment. We investigated the effect of EECP in patients with erectile dysfunction (ED). Thirteen patients were treated with EECP for 20 days, 1 h per day. Patients reported a significant improvement of penile rigidity after completion of the EECP treatment and a significant improvement of penile peak systolic flow was measured by Doppler sonography. No adverse effects were observed. In conclusion, EECP seems to be an effective treatment modality in patients with ED.


Background and hypothesis: Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for chronic angina. However, its usefulness has been felt to be limited in patients with angiographically demonstrated triple vessel coronary artery disease (CAD), in accord with the hypothesis that a patent vessel is necessary for transmission of the EECP-augmented coronary artery pressure and volume to the distal coronary vasculature. Methods: The effect of revascularization [coronary artery bypass grafting (CABG)] prior to EECP was examined in 60 patients with CAD and chronic angina (35 without and 25 with prior CABG). Patients were grouped by the extent of CAD (single-, double-, triple-vessel disease in the unrevascularized group) and by the extent of residual disease (number of stenotic native vessels unbypassed or supplied by a stenotic graft in the CABG group). Significant CAD or graft stenoses were defined as stenoses demonstrating ~ 70% luminal diameter narrowing. Benefit was assessed by improvement in post EECP treatment over pretreatment radionuclide stress testing. Results: Radionuclide stress testing demonstrated a comparable favorable response (80 vs.71%; p=NS) in patients with prior CABG versus unrevascularized patients. Enhanced external counterpulsation was highly and comparably effective in patients with unrevascularized native single- and double-vessel CAD and in patients with CABG with residual single-and double-vessel CAD (88 vs. 80%; p = NS). Most
notably, CABG significantly increased the beneficial response to EECP in those patients with triple-vessel CAD and stenotic grafts compared with unrevascularized patients with triple vessel CAD (80 vs. 22%; p<0.05 by chi-square test). Conclusion: The results suggest a new role for EECP as an effective treatment for post CABG ischemia, despite extensive CAD and even in the presence of stenotic grafts.


Background: Enhanced external counterpulsation (EECP) has been demonstrated to be an effective treatment for angina and exertional ischemia in patients with coronary disease. Hypothesis: It is hypothesized that the ability of EECP to enhance the recruitment or development of coronary collaterals in coronary artery disease may be determined by the relative magnitude of diastolic augmentation (DA) and systolic unloading (SU). This study examines the relation between the proposed EECP effectiveness ratio (DA/SU), as assessed by finger plethysmography, and changes in descending aortic flow as assessed by Doppler echocardiography in 15 patients during EECP. Methods: Varying external cuff pressures (0-275 mmHg) were used to generate a range of DA/SU ratios. The effect on aortic antegrade systolic and retrograde diastolic flow was assessed by Doppler echocardiography to determine whether there was an optimal EECP effectiveness ratio that maximizes the hemodynamic effects of EECP. With increasing DA/SU there was an initial positive linear increase in both systolic and diastolic flow volume. Systolic flow maximized at an effectiveness ratio of 1.5 and diastolic flow at a ratio of 2.0. Conclusion: Doppler ultrasonography was used to measure changes in the descending aortic flow that demonstrated that the hemodynamic effects of EECP are optimal for cuff pressure causing diastolic augmentation in the range of 1.5 and systolic unloading in the range of 2.0.


This paper summarizes the status of EECP in the treatment of patients with angina pectoris. It underlines the fact that this treatment is particularly indicated in patients at high risk for revascularization or for whom revascularization is not technically possible.


The article, through case studies, presents EECP as a convenient adjunct to the anti-ischemia armamentarium available at outpatient centers managing heart disease insofar as EECP is a non-invasive therapy that significantly improves myocardial perfusion and angina symptoms.

1997


This paper is presented as an overview of the Enhanced External Counterpulsation papers published in the October and November 1997 issue of Cardiovascular Reviews and Reports.


This review traces the evolution of external counterpulsation from its beginning to the early 1990s. The term counterpulsation derives from the dual hemodynamic goals of this treatment: to reduce the afterload of the left ventricle and to augment diastolic pressure. The studies summarized in this review demonstrate clinical benefits in the treatment of angina, acute myocardial infarction, and cardiogenic
It has been demonstrated that an external counterpulsation treatment system is highly effective when a series of 3 pneumatic cuffs is wrapped securely around the lower extremities and buttocks, inflating in a distal to proximal sequence, and deflating simultaneously timed to cardiac systole. Sequential inflation augments diastolic perfusion pressure; simultaneous deflation decreases peripheral vascular resistance, significantly decreasing cardiac workload. This method of counterpulsation, EECP, effectively increases myocardial oxygen supply by increasing coronary blood flow and diminishing myocardial oxygen requirements.


The effectiveness of EECP, a noninvasive outpatient treatment for angina pectoris, is described in this series of case reports from a community hospital. In a diverse patient population, EECP appears to provide significant relief of angina pectoris even in cases when CAD is fairly advanced and when other revascularization procedures have failed. The procedure appears most effective when at least one patent conduit, either graft or native coronary artery), can provide sufficient coronary flow to ischemic areas of myocardium. The benefits appear to be sustained over time.


EECP is a unique outpatient noninvasive treatment used to improve myocardial perfusion thereby reducing symptoms of obstructive CAD. EECP is a key component in the cardiovascular disease management program offered at The Heart-Lung Center, a comprehensive cardiopulmonary care center in Hawthorne, NJ. The center provides cost-effective preventive, educational and diagnostic services and treatments that have been shown to provide benefits in the evidence-based literature. EECP is used to stabilize the coronary circulation in patients with severe CAD. For many of the patients with chronic progressive CAD treated at the Heart-Lung Center, EECP has contributed to stabilization when maximal medical therapy and/or invasive procedures have proven inadequate. We believe this approach will translate into a reduction in hospital ER visits, inpatient admissions for chest pain, and of the need for and use of repeated costly and invasive forms of myocardial revascularization (PTCA and CABG). Three such cases are presented and discussed in this paper. Since EECP has demonstrated potential for stabilizing CAD this treatment is predicted to have an emerging role as an effective cardiovascular disease management tool to help providers of cardiac care share risk for the care of chronically and seriously ill patients with managed care organizations.


EECP (Vasomedical) is a noninvasive treatment that has shown promise in the treatment of ischemic coronary artery disease. Compared to the psychosocial sequelae of coronary bypass surgery and coronary angioplasty, EECP may offer certain psychosocial advantages that would contribute to improved quality of life in angina patients. Overall health perception and overall well being are enhanced greatly in subjects who show objective improvement in ischemia, and also in those without objective evidence of improvement. There are also improvements in depression scores in both subject groups. Given the predictive relationship between depression and mortality from cardiac disease, this may be an important finding to study further.

In U.S. clinical research, EECP (Vasomedical) has been shown to be an effective treatment for angina pectoris) with reported response rates ranging from a 75% success rates in unselected patients to 92% in patients with single vessel CAD. EECP effectively augments diastolic pressure and retrograde aortic flow) thereby increasing transmyocardial perfusion pressure. Demonstrable improvement of myocardial perfusion achieved by EECP may be due to collateral formation or recruitment. One or more proximally patent conduits (e.g., native coronary or bypass graft) improve the success of EECP, and is consistent with the concept that distal transmission of diastolic flow and pressure is necessary. Improvement in exercise tolerance after EECP may also be augmented by peripheral effects. The effects of EECP have been been shown to be maintained in a majority of responders over a 3-year period. Over a 4-7 year period, the majority of treated patients remained free of interim events or need for hospitalization, with mortality results comparable to reported historical medical and surgical treatment. The patients enrolled in the reported clinical trials present the full spectrum of CAD severity; from the patient with single vessel disease and good left ventricular function to the triple vessel disease patient with stenotic grafts and compromised left ventricular function. The reported findings support the effectiveness of EECP used in three strategies of CAD treatment. EECP is highly effective in lessening ischemic symptoms in the patient with single or double vessel disease who wishes to defer more aggressive means of revascularization. Also, it is effective as an adjunct to angioplasty or bypass grafting in patients with incomplete revascularization) further decreasing the ischemic burden. EECP finds its third clinical role in treating patients who are poor revascularization candidates because of comorbidity and technical reasons, though results in this group are less impressive.


There are many patients in whom repeat (or initial) PTCA and/or CABG are not appropriate and in whom aggressive medical therapy still fails to maintain a quality of life that patients are comfortable with. EECP is one of several new treatment alternatives for such patients. In our initial studies, 18 patients were treated with EECP for 1 hour daily for a total of 36 hours. All 18 patients experienced substantial improvements in anginal symptoms after EECP. Thallium-201 stress testing showed a complete resolution of ischemic defects in 12 patients (67%), a decrease in the area of ischemia in 2 patients (11%), and no change in 4 patients (22%). The long-term, sustained efficacy of EECP was confirmed in a 3-year follow-up study. One possible explanation for the improvement in perfusion that we observed is that EECP may open, or enhance the development of, collateral channels when at least 1 patent conduit (native vessel or bypass graft) is present. The importance of having such a conduit was emphasized in our most recent study of 50 patients, all of whom underwent coronary angiography before EECP.


Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for chronic stable angina. Despite intensive risk factor modification, a patient required two surgical coronary revascularizations and seven multivessel angioplasties over a 26-month period, demonstrating recurrent unstable angina and persistent thallium perfusion defects despite revascularization. Post EECP, angina was relieved, thallium defects were resolved and the patient has remained asymptomatic for 36 months.

1996


Patient Population Fifty patients (46 men, 4 women, mean age 61 yrs) with chronic stable angina and evidence of reversible radionuclide stress perfusion defects and angiographic coronary disease (>70% stenosis in a major coronary vessel) were divided into three groups: 1-, 2-, and 3-vessel disease.
Information about prior myocardial infarction, revascularization, cardiac risk factors and current medications were obtained. Treatment protocol: Daily 1- to 2-hour EECP sessions 5 days a week to a total of 35 hours. Measurements Repeat radionuclide perfusion stress testing to the same cardiac workload as baseline was performed within one week of cessation of EECP. Pre- and post-EECP radionuclide stress perfusion images were evaluated by two independent interpreters blinded to patient identities and graded as being unchanged or showing partial or complete resolution of reversible perfusion defects. Results There was a significant difference between pre- and post-EECP radionuclide stress perfusion imaging (p<0.001). There was a significant inverse relationship between the extent of coronary artery disease and therapeutic benefit by changes in stress radionuclide perfusion images. Perfusion defects improved in 95% of patients (18/19) with 1-vessel coronary artery disease, in 90% of patients (17/19) with 2-vessel disease, and only 42% of patients (5/12) with 3-vessel disease. Cardiac risk factors, age, prior myocardial infarction, and ejection fraction were not significantly correlated with the response to EECP therapy.


Patient Population: 27 patients (26 men, 1 woman, mean age of 60) with chronic stable angina and evidence of ischemia demonstrated by maximal radionuclide stress perfusion using the Bruce protocol. Treatment protocol: Daily 1- to 2-hour EECP sessions 5 days a week to a total of 36 hours. Measurements: Pre- and post-EECP radionuclide stress test to the cardiac workload at baseline, and an additional maximal treadmill stress test performed within one week after the end of treatment. Radionuclide images were independently evaluated by two observers blinded to patient identity and classified as being unimproved or improved (partial or complete resolution of reversible perfusion defects). Results Exercise duration improved significantly from 7.17±0.53 minutes before EECP to 8.84±0.49 minutes after EECP (p<0.0001). An improved exercise tolerance was seen after treatment in 22 out of 27 patients (81%). Pre- and post-EECP heart rate, blood pressure and double product did not change significantly. A subgroup of patients with improved post-EECP perfusion imaging demonstrated significant increases in maximal exercise duration (9.12±0.60 vs. 7.22±0.63 minutes, p<0.0005) and peak heart rate from (127.9±5.7 vs. 117.8±6.0 beats/min, p<0.05). Peak blood pressure and double product did not differ significantly between pre- and post EECP testing. In the subgroup of patients with unimproved post-EECP perfusion imaging, there were no significant differences in maximal exercise duration, peak heart rate, and peak blood pressure. However, there was a significant decrease in post-EECP maximal double product. Comparison of the improved and unimproved subgroup of patients 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. However, there was no significant difference in the change in exercise duration between the two groups.


Patient Population: Sixteen patients (15 men and 1 woman). Treatment Protocol EECP was applied in an out-patient setting while measurements were made. Measurements: Patients were evaluated at rest and during EECP treatment using Doppler echocardiography. Pulsed Doppler measurements of flow in the descending aorta were made at a fixed depth setting from the suprasternal notch using a Hewlett-Packard Sonos 1500 ultrasound system. Results There was an increase in the systolic time velocity integral (STVI), representing cardiac output, and the diastolic time velocity integral (DTVI, representing retrograde flow in the aorta during diastole. A 60% change in cardiac output was noted during EECP as compared with resting and there was a 227% increase in average retrograde flow. Results for each measurement are expressed in the following table as mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>During EECP</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>64.3±6.8</td>
<td>69.2±7.5</td>
<td>NS</td>
</tr>
<tr>
<td>STVI (cm)</td>
<td>14.2±6.5</td>
<td>21.5±8.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DTVI (cm)</td>
<td>1.7±1.5</td>
<td>8.3±3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D/S TVI</td>
<td>0.17±0.16</td>
<td>0.40±0.11</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
1995


Patient Population: 18 patients with chronic angina treated with EECP from 3/1989 to 5/1991 (reported in *Am J Cardiol* 1992; 70:859-862). 17 patients were contacted, 1 patient could not be located.

Treatment protocol: Daily 1-hour EECP sessions 5 days a week to a total of 36 hours. Measurements of the 17 patients contacted, 12 patients performed repeated stress thallium perfusion treadmill tests to the same exercise level as their pre-EECP perfusion studies, 1 patient refused, and the 4 remaining patients were excluded from repeated stress tests because of interim events. Results: 17 patients were free of angina 3 years after EECP treatment, but 4 patients had interim events (2 CABG, 1 PTCA and 1 MI). 8 of 12 patients who had achieved complete resolution of their ischemic perfusion defects immediately after EECP treatment showed sustained improvement in their 3-year follow-up stress thallium perfusion; 1 patient reverted to baseline (pre-EECP) perfusion defects; 2 patients had intercurrent events, and 1 patient was lost to the study. Of the 2 patients who had achieved partial resolution after EECP, 1 of the 2 patients who had achieved partial resolution after EECP reverted to baseline and the other refused repeat stress perfusion study. Of 4 patients with unchanged stress thallium perfusion defects after their EECP treatment, 2 had the same defects in their repeated stress thallium perfusion, and the remaining 2 patients had intercurrent events.


Patient Population 12/18 patients treated with EECP from 3/1989 to 5/1991 (reported in *Am J Cardiol* 1992; 70:859-862). Treatment protocol: Daily 1-hour EECP sessions 5 days a week to a total of 36 hours. Measurements of the 12 patients were given a psychosocial battery 1 day prior to the start of EECP and on the last day of treatment. This included the Psychosocial Adjustment to Illness Scale-Revised (PAIS-R) and a questionnaire on pain, exercise, and medication needs. Results One out of the seven subscales of adjustment on PAIS-R questionnaires reached statistical significance. However, values for both pre- and post-EECP were generally below the mid-point (t=50), demonstrating a relatively good overall adjustment of the patients to their illness and showing that the EECP treatment did not change their adjustment to illness, with a reduction in their psychological distress. Subjective pain ratings on 9 patients demonstrated a significant decrease in the frequency of chest pain (p<0.01) as well as in the pain’s severity (p<0.05). Patients’ use of nitrates to alleviate pain decreased as well (p<0.01). All of the patients reported an improvement in their ability to work, in energy levels, and in their overall well-being.


We report our experience using the new noninvasive treatment for coronary patients called enhanced external counterpulsation (EECP). Thallium-201 stress scintigraphy and treadmill test were done before and after 36 sessions of EECP treatment on 38 coronary patients. The results showed significant (p<0.01) improvement in perfusion as well as exercise tolerance in 86.8% and 94.2% of patients respectively. The symptoms of angina pectoris and functional classes of the patients also showed significant (p < 0.05) improvement. All patients tolerated the treatment without serious complications. The magnitude and rate of increased exercise tolerance achieved by EECP treatment was greater than those achieved by training after coronary bypass surgery (CABG) or exercise training rehabilitation program for the matched coronary patients reported by others. The mean double products (DP) from the treadmill test results of the improved TI-201 perfusion subgroups decreased significantly (p < 0.001). On the contrary, the DP of the unimproved subgroup increased significantly (p<0.001). This could mean improvement in efficiency of the heart in the former, that is, more work was done with lower pressure-pulse products.
1994


Enhanced external counterpulsation (EECP) is a noninvasive procedure, in which compressions are applied to the vascular beds within the muscles of the legs, thighs, and buttocks in a sequential manner, progressing from the calves upward. Prompted by favorable results with EECP in Chinese angina patients, we studied the efficacy of the technique in 18 patients with chronic stable angina and evidence of exertional ischemia by thallium-201 perfusion imaging. Patients received 1 hour of EECP therapy daily for a total of 36 hours. Treatment with EECP produced substantial improvements in symptoms in all 18 patients and reduced myocardial ischemia, as assessed by thallium scanning, in 14 patients. Follow-up of 17 patients showed that the subjective and objective benefits of EECP were maintained for at least 3 years in most patients. In selected angina patients, EECP should be seriously considered as part of the treatment program.

1992


Patient Population: 18 patients with chronic stable angina, 8 with 19 prior revascularization attempts, 7 with a total of 14 myocardial infarctions. All patients had evidence of exertional ischemia by baseline pre-EECP maximal stress thallium-201 perfusion imaging with Bruce protocol. Treatment protocol: Daily 1-hour EECP sessions 5 days a week to a total of 35 hours. Measurements Pre- and post-EECP exercise stress thallium-201 perfusion imaging performed to the same exercise duration as pre-EECP. Results 18/18 patients reported noticeable improvement in angina; 16 had complete relief during usual activity. There was a significant decrease in thallium perfusion defects post-EECP (p<0.01, Chi-square statistical analysis). 12/18 patients (67%) showed complete resolution of their thallium ischemic reversible defects, while 2/18 patients (11%) showed partial resolution, and 4/18 patients (22%) showed unchanged thallium defects. Significant increase in post-EECP maximal exercise duration (9.72 ± 0.77 minutes) when compared with pre-EECP (9.72±0.77 vs. 8.14±0.71 minutes, p<0.005). 13/14 patients (93%) with improved thallium perfusion imaging demonstrated significant improvement in both exercise tolerance and double product attained.