External Counterpulsation Produces a Significant Reduction in Stable Angina Class, Episodes, Medication Use, and Hospitalization

The authors performed a multicenter, retrospective assessment of data from 58 patients with Canadian Cardiovascular Society (CCS) functional class II (n=27), class III (n=23), or class IV (n=8) chronic, stable angina and documented coronary artery disease who were serially treated with the CardiAssistTM External Counterpulsation System (ECP) (Cardiomedics, Inc., Irvine, CA). All of the patients received 30–35 treatments of one hour/day over a 6–7-week period. The ECP System reduced angina in CCS class II, class III, and class IV stable angina patients by an average of one CCS class, lowered the incidence of anginal episodes in 91% of the patients (53 of 58), and resulted in a 96% reduction in the number of patients requiring hospitalization for angina, from 24 in the 6 months pretreatment to one patient in the 6 months post-treatment. (CVR&R. 2001; 22:154–158)

Gerald Weisfogel, MD;[1] Martin Schaffer, MD;[2] Dietmar Gann, MD;[3] Berge Dadourian, MD;[2] Timothy Marshall, MD;[3] V. Allymadian, MD[4]
From Metuchen Heart Associates, PA, Metuchen, NJ;[1] Nevada Cardiology Associates, Las Vegas, NE;[2] Tucson Heart Group, Tucson, AZ;[3] and Orange County Thoracic & Cardiovascular Surgeons, Orange, CA[4]

Address for correspondence/reprint requests: Gerald Weisfogel, MD, ECP Center of New Jersey, 42 Throckmorton Avenue, Old Bridge, NJ 08857
Manuscript received June 29, 2000; accepted July 31, 2000

External counterpulsation (ECP) is a noninvasive treatment for coronary artery disease. The CardiAssist™ ECP System employs the sequential inflation of pneumatic cuffs about the calves, thighs, and buttocks to augment diastolic pressure and increase venous return to the heart, decreasing left ventricular afterload. Augmenting diastolic pressure increases coronary artery perfusion pressure and possibly enhances coronary collateral development, resulting in the reduction or elimination of the ischemia associated with episodes of angina.

Historical Perspective

The concept of counterpulsation was first introduced in the U.S. in 1953, when Kantrowitz and Kantrowitz[1] proposed that elevation of aortic diastolic pressure could improve coronary blood flow and benefit patients with coronary insufficiency. Several early ECP devices increased coronary blood flow and demonstrated hemodynamic benefits. However, their usefulness in clinical practice has been limited because of numerous obstacles, including patient comfort, risk of electric shock, and economics. The first ECP systems consisted of a hydraulically driven device with water-filled bladders that were wrapped around the lower legs and thighs.

ECP in Acute Myocardial Infarction

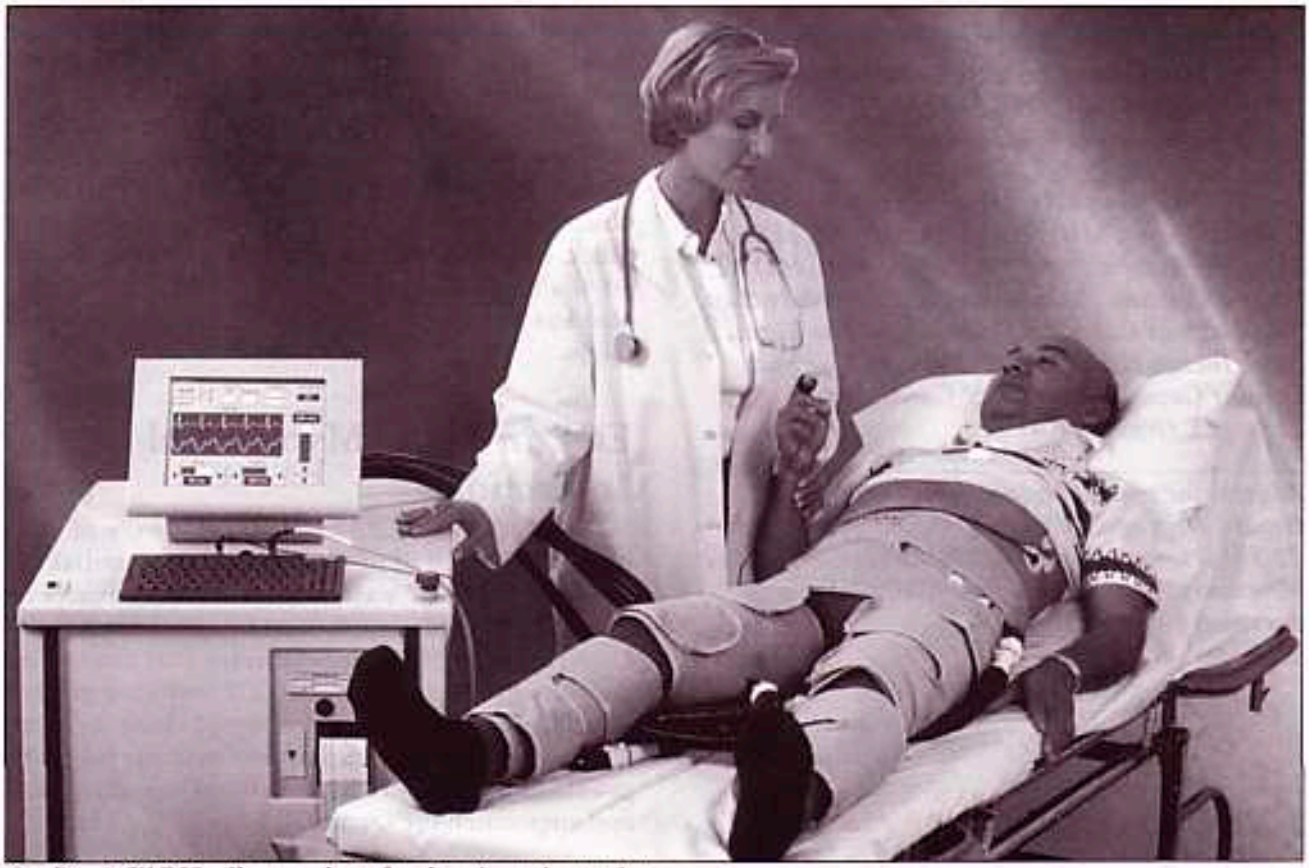
In 1972, Mueller et al.[2] first studied the use of ECP in the treatment of uncomplicated myocardial infarction (MI). ECP was associated with increases in diastolic pressure and in coronary blood flow. Later, Parmley et al.[3] demonstrated that combining the use of nitroprusside and ECP provided greater benefits than the use of either agent alone. ECP reversed the decrease in diastolic arterial pressure produced by nitroprusside-induced vasodilatation and augmented the cardiac index.

ECP in the Treatment of Angina

Over the past two decades, a number of studies have suggested the efficacy of ECP in the treatment of patients with chronic stable angina.[4–7] The first sham-controlled study, reported by Clapp et al.[8] in 1974, using a predecessor of the current CardiAssist™ System, demonstrated improvement in functional classification, nitrate usage, and double product. In a subsequent study published in 1999, Arora et al.[9] concluded that enhanced ECP (EECP®, distributed by Vasomedical, Inc., Westbury, NY) reduced angina and extended time to exercise-induced ischemia in 139 patients with symptomatic coronary artery disease (CAD); exercise duration increased in both active groups, but not significantly.[9]

Methods

Subjects. At four cardiology practices that served as study sites (see Appendix), data were collected on every patient treated with the CardiAssist™ ECP System between June, 1997 and April, 1999 who met the following criteria: age 40–90 years; angina classified as Canadian Cardiovascular Society (CCS) functional class II, III, or IV; documented evidence of CAD; and 30–35 1-hour treatments with the CardiAssist™ System. Documentation of CAD required that a patient have at least one of the following: angiographically proved stenosis of greater than 70% in at least one of the major arteries, and/or a history of MI documented by characteristic creatinine kinase elevation and development of Q waves on electrocardiography. Data were extracted from treatment forms used by each of the sites that administered the CardiAssist™ treatment regimen. When the treatment form did not provide the necessary data, they were obtained at the study site from the patient's complete medical record. The study sites routinely exclude patients from treatment if they have any of the following: CCS class I or unstable angina; MI or CABG in the preceding 3 months; cardiac catheterization in the preceding 2 weeks; overt congestive heart failure or a left ventricular ejection fraction of <30%; blood pressure of >180/100 mm Hg; a permanent pacemaker or implantable defibrillator; significant valvular heart disease; a history of varicosities, deep vein thrombosis, phlebitis, or stasis ulcer; atrial fibrillation or frequent ventricular premature beats; bleeding diathesis; or current pregnancy. CCS class III and IV patients were selected who were not surgical candidates because their conditions were inoperable or they were at high risk of operative complications or postoperative failure, had coronary anatomy that was not readily amenable to such proce-



CardiAssist™ ECP offers new hope for chronic angina patients.

dures, or had comorbid conditions that created excessive risk. CCS class II patients were selected according to the same criteria or if they refused interventional procedures.

CardiAssist™ ECP System. The CardiAssist™ System is an enhanced version of the original ECP device (Cardiomedics, Inc., Irvine, CA). The system consists of a console containing air compressors, a computerized touch screen control console, valves, hoses, and three sets of cuffs. Prior to the beginning of a treatment session, the cuffs are wrapped around the patient's legs and buttocks and fastened with Velcro® (DuPont Corporation). Pressure is applied via compressed air to the cuffs in the following sequence: calves, thighs, and buttocks, in synchronization with the "r" wave of the patient's electrocardiogram. This propels arterial blood back to the coronary arteries and heart muscle. Before the end of diastole, all air is released simultaneously from all cuffs by removal of the externally applied pressure. This allows the compressed arteries and veins to reconform, reducing vascular impedance. Pressures that can be applied range from 0–310 mm Hg. Patients in this study received 250–310 mm Hg pressure. Blood pressure changes were monitored by finger plethysmography. Assessment of the hemodynamic effect of the CardiAssist™ System is calculated via the device's Central Processing Unit (CPU), using the systolic and diastolic peak wave heights. A systolic to diastolic ratio equal to or greater than 1 (diastolic pressure equal to or greater than systolic pressure) is generally considered therapeutic. In this study, the average diastolic to systolic pressure ratio was 1.1 (high of 1.9, low of 0.4).

End Points. CCS functional class was determined prior to treatment and compared mathematically to the ending CCS class. Angina episodes, rehospitalization for angina, and angina medication consumption were recorded daily. During the treatment period of 6–7 weeks, events were tabulated and reported at the conclusion of treatments as "increased," "decreased," or "no change." The average frequency of angina episodes per day was computed by dividing the total number of angina episodes over a 1-week period both pre- and post-treatment. In addition, the difference in frequency of angina episodes between pretreatment and the end of treatment was calculated as percentage change and categorized as follows: 50%+, 25%–49%, and 0%–24% improvement. No patient's condition was worse after treatment; all patients treated with the CardiAssist™ System in this study displayed improvement in at least one of the parameters listed above.

Statistical Analysis. Analysis of variance, pretreatment vs. post-treatment, was performed to determine the F ratio, as well as a single variable test with a 0.05 level of significance. Changes in the incidence of angina episodes from pre- to post-treatment and thorough follow-up were analyzed by analysis of variance, and differences between groups with respect to percentage changes in the number of angina episodes were determined. Other observed factors (rehospitalization for angina, angina medication consumption, and CCS classification) were also assessed by computing percentage changes.

TABLE I. PATIENT CHARCTERISTICS

NUMBER	58
Age in years (mean±SD)	(70±10)
Male	42 (72%)
Female	16 (28%)
CARDIOVASCULAR HISTORY	
CCS functional class	
II	27 (46%)
III	23 (40%)
IV	8 (14%)
Previous CABG	15 (26%)
Previous PTCA	14 (24%)
Multiple procedures	9 (16%)
CARDIOVASCULAR MEDICATIONS	
Nitrates	51 (88%)

CCS=Canadian Cardiology Society; CABG=coronary artery bypass grafting; PTCA=percutaneous transluminal

TABLE II. CANADIAN CARDIOLOGY SOCIETY FUNCTIONAL CLASSIFICATION

Number	Pretreatment Functional Class	Post-Treatment Functional Class	*p* Value
58	2.67±0.71	1.71±0.65	7.32×10^{-12}

TABLE III. PERCENT IMPROVEMENT IN ANGINA SYMPTOMS

Number	50+%	25%–49%	0%–24%
58	42	11	5

TABLE IV. AVERAGE NUMBER OF ANGINA EPISODES OVER 24 HOURS

Number	Pretreatment Angina	Post-Treatment Angina	*p* Value
58	1.59±2.86	0.31±0.57	0.001

TABLE V. HOSPITALIZATIONS PER PATIENT OVER 6 MONTHS OF FOLLOW-UP

Number	Pretreatment	Post-Treatment	*p* Value
24	1.17±038	0.04±0.20	1.02 x 10-16

Results

Patient Characteristics. Of the 58 patients, 54 received 35 1-hour treatments over a 7-week period. Four patients received <35 treatments (30, 31, 33, and 34). The average age was 70 (oldest, 90; youngest, 47). Forty-two patients were male (72%) and 16 female (28%). Twenty-seven patients were CCS class II (46%), 23 were CCS class III (40%), and eight were class IV (14%). Twenty-nine of the 58 patients (50%) had undergone prior invasive procedures, such as coronary artery bypass grafting (CABG) or angioplasty. Nine patients (16%) had previously undergone multiple CABG, percutaneous transluminal coronary angioplasty (PTCA), and/or stenting. These data are shown in Table I.

CCS Functional Class. Changes in functional class are shown in Table II. The eight class IV patients improved by an average of 1.7 CCS classes (4.0 to 2.3). There was a 44% average improvement in the class IV patients (50% improvement in six and 25% improvement in the remaining two patients). The 23 class III patients improved by an average of 0.9 class (3.0 to 2.1), the average improvement being 29% (four showed no improvement, 18 showed 33% improvement, and one showed an improvement of 67%). The 27 class II patients improved by an average of 0.8 class (2.0 to 1.2). There was 41% improvement on average among the 27 class II patients (22 showed an improvement of 50%, while five patients showed no improvement). All of the eight CCS class IV patients, 83% of class III patients (19 of 23), and 81% of class II patients (22 of 27) improved in terms of CCS functional classification. For the entire group of 58 patients, the CCS class was reduced from 2.67 to 1.71. Overall, 84% of the patients (49 of 58) experienced a reduction in their CCS classifications, while 16% (nine of 58) showed no improvement.

Angina Incidence. Fifty-three of the 58 patients (91%) experienced a reduction in their angina episodes post-treatment, from an average of 1.59±2.86 episodes per 24-hour period to 0.31±0.57 episodes per 24-hour period. Forty-two of the 58 patients (72%) had a significant decrease in the number of angina episodes and were calculated to have achieved 50%+ improvement. Eleven patients (19%) showed a 25%–49% reduction in angina episodes, while five patients (9%) fell into the 0%–24% category. No patient had an increase in the frequency of angina episodes. These results are given in Tables III and IV.

Hospitalization Incidence. Twenty-three of the 24 patients (96%) who had been hospitalized in the 6-month period before treatment reduced their hospitalization rate for angina to zero in the 6 months following treatment (Table V).

Nitroglycerin Usage. As detailed in Table VI, consumption of angina medication (expressed as the number of times taken per 24 hours) decreased by 77.4%, from an average of 0.62±0.71 pretreatment to an average of 0.14±0.33 post-treatment.

TABLE VI. SUBLINGUAL NITROGLYCERIN CONSUMPTION PER DAY

Number	Pretreatment	Post-Treatment	*p* Value
58	0.62±0.71	0.14±0.33	7.94×10^{-6}

TABLE VII. CANADIAN CARDIOVASCULAR SOCIETY FUNCTIONAL CLASSIFICATION

Class	Description
Class I	Ordinary physical activity does not cause angina. Angina with strenuous, rapid, or prolonged exertion at work or recreation.
Class II	Slight limitation of ordinary activity. Angina with walking or climbing stairs rapidly. Walking uphill, walking or stair climbing after meals. Walking in cold or wind, or under emotional stress. During the few hours after awakening. Walking more than two blocks on level ground and climbing more than one flight of ordinary stairs at a normal pace and under normal conditions.
Class III	Marked limitation of ordinary physical activity. Angina with walking 1–2 blocks on level ground and climbing one flight of stairs under normal conditions and at a normal pace.
Class IV	Inability to carry on any minimal physical activity without discomfort. Anginal syndrome may be present at rest.

Discussion

Study Limitations. The sample size was relatively small and this study was not randomized or blinded. The long-term effects of ECP on symptoms and clinical events are unknown, although it is encouraging that 14–24 months post-treatment most patients continue to have relief. Despite the lack of controls, the results actually reflect a lack of bias, as the studied cohort was a population treated consecutively based on accepted inclusion/exclusion criteria for patients at very high risk for additional operative procedures or whose anatomy was not amenable to invasive procedures. All patients who met the inclusion criteria were treated. The findings of this study mirror many of the recently reported results of the MUlticenter STudy of Enhanced ECP (the MUST-EECP trial),[9] a prospective, randomized, blinded study.

Possible Clinical Implications. CAD is chronic in nature. Normally, long-term survival can be extended if some type of secondary intervention/prevention can be applied. The practitioners in these study centers routinely see patients with recurrent stable angina despite current or previous therapy with anti-ischemic agents and various revascularization attempts. The patients in this study fall into this category and thus it would seem that ECP may offer an additional treatment option.

Conclusion

One of the authors' motivations was to determine if daily application of ECP therapy in a normal clinical setting would produce results similar to those obtained in a controlled, scientific study setting. Despite the shortcomings mentioned above, it is comforting to have found that an ECP system applied in a real-world treatment setting provided excellent results for a large angina patient population. A body of data, including this study, demonstrates that ECP, delivered pneumatically in a sequential manner via cuffs encircling the lower extremities (calves, thighs, and buttock area), is an effective therapy for patients with chronic stable angina.

Appendix: ECP Center of New Jersey, 42 Throckmorton Avenue, Old Bridge, NJ 08857, 732-679-7972—Nevada Cardiology Associates, 3150 N. Tenaya Way, Ste. 460, Las Vegas, NV 89128, 702-233-1000—Tucson Heart Group, 4892 North Stone, Tucson, AZ 85704, 520-696-4780—Orange County Thoracic and Cardiovascular Surgeons, 1310 West Stewart Drive, Ste. 502, Orange, CA 92868, 714-997-2224.

References

1 Kantrowitz A, Kantrowitz A. Experimental augmentation of coronary flow by retardation of arterial pressure pulse. *Surgery*. 1953;34:678–687.
2 Mueller H, Ayres S, Grace W, et al. ECP: A non-invasive method to protect ischemic myocardium in man [abstract]. *Circulation*. 1972;46(suppl):II–19.
3 Parmley WW, Chatterjee K, Charuzi Y, et al. Hemodynamic effects of noninvasive systolic unloading (nitroprusside) and diastolic augmentation (ECP) in patients with acute myocardial infarction. *Am J Cardiol*. 1974;33:819–825.
4 Zheng AX, Li TM, Kambic H, et al. Sequential ECP (SECP) in China. *Trans Am Soc Artif Intern Organs*. 1983;29:593–603.
5 Lawson W, Hui JC, Burger L, et al. Improved exercise tolerance following enhanced ECP: Cardiac or peripheral effect. *Cardiology*. 1996;87:271–275.
6 Lawson W, Hui JC, Sorrell HS, et al. Efficacy of enhanced ECP in the treatment of angina pectoris. *Am J Cardiol*. 1992;70:859–862.
7 Banas JS, Brilla A, Levine HJ. Evaluation of ECP for the treatment of angina pectoris [abstract]. *Am J Cardiol*. 1973;31:118.
8 Clapp JC, Banas JS, Stickley LP, et al. Evaluation of sham and true ECP in patients with angina pectoris. *Circulation*. 1974;50(suppl):III–108.
9 Arora RR, Chou TM, Jain D, et al. The Multicenter Study of Enhanced ECP (MUST-EECP): Effect of EECP on exercise-induced myocardial ischemia and anginal episodes. *J Am Coll Cardiol*. 1999;33:1833–1840.