

An Analysis of the Efficacy and Safety of Enhanced External Counterpulsation at West Virginia University Hospitals

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Abstract

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 < .05, Wilcoxon Signed-Rank test). Overall, EECP was effective in improving angina as reflected in a substantial reduction in anti-angina medications in 59 (75%) patients.

Introduction

Enhanced external counterpulsation (EECP) is gaining increasing acceptance as a non-invasive outpatient treatment for angina pectoris refractory to standard medical therapy (1,2,14). Data reported in the clinical literature provide compelling evidence supporting the safety and efficacy of this modality in selected study subjects enrolled in clinical trials (1,2,3). However, it is still an evolving issue about which patients are likely to benefit. Conversely, which patients are more likely to suffer adverse effects and which are less likely to suffer from the procedure is also not well defined.

West Virginia University Hospitals is one of the first facilities in the state to perform EECP. We performed a retrospective analysis of the first 79 consecutive patients who underwent EECP at WVUH in an effort to identify those individuals for whom this procedure is most appropriate and those for whom EECP is either ineffective or harmful.

Methods

A retrospective analysis was performed of 79 consecutive patients (87% men and 13% women) who underwent EECP at West Virginia University Hospital for treatment of refractory angina during the period from November 1998 through September 2005. The study was approved by the Institutional Review Board for the Protection of Human

Subjects at West Virginia University. Permission was requested to evaluate medical records to analyze clinical data. Phone calls were also made to selected patients if such information was unavailable from the clinic chart. Phone calls consisted of a phone script that was read to patients regarding the study and a phone survey that was answered by patients. Phone numbers were obtained through the West Virginia University Hospital medical records.

A chart review and/or phone survey was conducted on all patients who received EECP treatment to determine age, gender, race, risk factors for heart disease, history of myocardial infarction, coronary anatomy, medication history, left ventricular function, and history of cardiac catheterization, percutaneous coronary intervention or coronary artery bypass graft surgery. Assessment of favorable and/or adverse effects of treatment were similarly established.

EECP was performed as previously described in accordance with the manufacturer's recommendations (17). EECP is a non-invasive outpatient treatment utilizing three, paired, inflatable cuffs wrapped around the lower extremities for approximately 1-2 hrs. a day, 5 days a week for 7 weeks (35 treatments). The cuffs are sequentially inflated during the cardiac cycle in the calves first, followed by the lower thighs, and then the upper thighs. The pressure is released at the beginning of the next cardiac cycle. Compressions are electronically gated to the diastolic portion of the cardiac cycle determined by ECG.

Each patient was seen by a nurse and a physician and routinely monitored by electrocardiogram and pulse oximetry. Initial and interval histories were recorded for each patient before and after each treatment. The history included the angina functional class, angina frequency, nitroglycerin use, changes in medication, and potential side effects of the treatment.

Table 1. Patient Characteristics and Medical History.

Variable	n=79
White	74 (94%)
Male	69 (87%)
Female	10 (13%)
<50 yo	12 (15%)
50-75 yo	55 (70%)
>75 yo	12 (15%)
Hypertension	74 (94%)
Diabetes Mellitus	34 (43%)
Hyperlipidemia	69 (87%)
Family History of CAD	47 (59%)
Past or Present Smoking	40 (51%)
Peripheral Vascular Disease	19 (24%)
Prior Myocardial Infarction	48 (61%)
History of Arrhythmia	13 (16%)
LVEF < 40%	20 (25%)
Diastolic Heart Failure	7 (9%)
Prior coronary intervention	52 (66%)
Prior coronary bypass	70 (89%)
Redo coronary bypass	7 (9%)

Table 2. Medication History.

Variable	n=79
Beta Blockers	70 (89%)
Nitrates	64 (81%)
Ace Inhibitors	53 (67%)
Aspirin	58 (73%)
Calcium Channel Blockers	50 (63%)
Angiotensin Receptor Blockers	3 (4%)
Lipid Lowering Medications	57 (72%)

Table 3. Side Effect Profile During EECP.

Variable	n=79
Chest pain	2 (2.5%)
Shortness of Breath	1 (1.3%)
Leg pain/numbness	3 (3.8%)
Acute MI	1 (1.3%)
Lower extremity clot	1 (1.3%)
Rheumatoid Arthritis pain	1 (1.3%)
Hip Pain	1 (1.3%)
Noncardiac hospitalization	2 (2.5%)

Comparisons between pre and post scores were made by the Wilcoxon Signed-Rank test. Means, both pre and post treatment, were reported for the group as a whole and for various subgroups. P-values < 0.05 were taken as significant evidence of a difference between groups.

Results

A total of 79 patients were referred to West Virginia University Hospitals for EECP. All patients had angina on entry with Canadian Cardiovascular Society (CCS) functional classes ranging from II-IV (2). They were predominantly white (94%), but also included Asians (2.5%) and Hispanics (3.8%). There were 87% men and 13% women. Most patients ranged in age from 50-74 years (70%); while 15% were less than 50 years of age and 15% older than 75 years (Table 1). All patients were considered by the referring cardiologist to have had angina refractory to maximal medical therapy prior to EECP treatment (Table 2).

A total of 60 (76%) patients who were referred for EECP successfully finished the 35 treatments. Most (92%) were in either CCS Class III or IV at baseline, but very few (6%) remained in either CCS Class III or IV at the end of treatment. 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. Another 7 patients failed to complete all 35 sessions because of transportation problems or because they declined further treatment. Major adverse cardiovascular events occurring over the course of therapy were uncommon and included: chest pain (2.5%), shortness of breath (1.3%), acute MI (1.3%), and lower extremity vascular occlusion (1.3%) (Table 3).

There was a statistically significant improvement in angina class and reduction in anti-angina medication in those who completed a full course of EECP treatment. Overall, EECP was effective in improving angina as reflected in a substantial reduction in anti-angina medication in 59 (75%) patients.

Similar statistically significant improvements in angina class and reduction in anti-angina medication were observed in every co-morbid subgroup analyzed, including patients with peripheral vascular disease, diabetes, hyperlipidemia, hypertension, smoking, Post-MI, and LVEF < 40% (P < .05, Wilcoxon Signed-Rank test).

Discussion

The efficacy of EECP at West Virginia University Hospitals is consistent with the published literature (1,2,3,7,12). The MUST-EECP trial was the first prospective, randomized, blinded, controlled study of EECP. In it, 75% of patients had both an improvement in

radionuclide stress perfusion imaging and treadmill exercise duration on a Bruce protocol following treatment.

Lawson et al found that 74% of 2,289 patients enrolled in the EECP Consortium who were in CCS angina classes II-IV improved at least one functional class. Nearly 40% of patients in CCS class III-IV improved two or more angina classes. There was a 4.0% rate of adverse experiences after the treatment. Both men and women responded to the treatment equally (2). Michaels et al found a 73% reduction of > 1 angina class among 1,097 patients after EECP that persisted for at least two years. In addition, 50% of patients reported an improvement in quality-of-life assessment after EECP that was also sustained at two years of follow-up (3).

Our study showed significant benefit in reduction of anti-angina medications in our patients at West Virginia University following a full course of 35 hours of EECP treatment. Reports by others in the clinical literature support the requirement for a full 35 hours of treatment (2,17). Less than the full 35-hour treatment is associated with a decreased probability of improvement (2). Interestingly, a potential for greater efficacy by exceeding the current 35 hours of treatment has not been reported. Improvement in both CCS functional class and reduction in anti-angina medication following EECP was consistent in all sub-groups analyzed.

These results show that EECP is an effective non-invasive treatment for patients with coronary artery disease refractory to medical treatment.

Patients usually tolerate the procedure well with a low risk of side effects from the treatment. Previous studies have also documented a low morbidity associated with EECP treatment (1,2,4). Twelve patients in our study had side effects, mostly related to lower extremity trauma or bruising. However, one patient developed acute myocardial infarction after the 17th treatment. We cannot include or exclude a potential role for EECP in this complication.

The contraindications to EECP treatment include the following: arrhythmias that interfere with machine triggering, a bleeding diathesis, active thrombophlebitis, severe lower extremity vaso-occlusive disease, presence of a documented aortic aneurysm requiring surgical repair, and pregnancy (17). Old age is not specifically excluded. However, the elderly often do not receive more aggressive and/or new treatments due to concerns about potential side effects and/or lack of efficacy. In our experience, individuals over 75 years (12 patients) did well with respect to side effects. Only 2 were unable to finish the treatment (one patient was admitted to the ICU for a pneumonia and one patient was admitted for an acute MI). Nine of the 12 patients who completed the full course benefitted. Thus, patients of advanced age should not be denied the potential benefits of EECP.

Conclusion

Patients tolerate EECP well and benefit from the treatment, as reflected in a decrease in the frequency of angina and reduction in sublingual nitrate use. Potential mechanism(s) responsible for the benefits derived from EECP are still largely unknown. The three most widely posed hypotheses include an increase in diastolic coronary artery flow, changes in neurohormonal mechanisms, and intrinsic changes in left ventricular function independent of changes in the cardiac load (9). Studies are now under way at West Virginia University to elucidate the mechanisms contributing to the efficacy of this treatment.

References

1. Lawson WE. Analysis of baseline factors associated with reduction in chest pain in patients with angina pectoris treated by enhanced external counterpulsation. *Am J Cardiology*. 2003; 92:439-442.
2. Lawson WE, Hui JCK, Lang GR, et al. Treatment benefit in the enhanced external counterpulsation consortium. *Cardiology*. 2000;94:31-35.
3. Michaels AD. Two-year outcomes after enhanced external counterpulsation for stable angina pectoris (from the International EECP Patient Registry [IEPR]). *Am J of Cardiology*. 2004;93:461-464.
4. Arora RR. Effects of enhanced external counterpulsation on health-related quality of life continue 12 months after treatment: a sub study of the Multicenter Study of Enhanced External Counterpulsation. *J of Investigative Med*. 2002; 50: 25-31.
5. Feldman AM. Enhanced external counterpulsation: mechanism of action. *Clin Cardiol*. Dec 2002; 25 (suppl II): 11-15.

6. Conti CR. Ongoing and planned studies of enhanced external counterpulsation. *Clin Cardiol*. Dec 2002; 25 (suppl. II): II-26-II-28.
7. Beller GA. A review of enhanced external counterpulsation clinical trials. *Clin Cardiology*. Dec 2002; 25 (suppl. II): II-6-II-10.
8. Sinval RM. Enhanced external counterpulsation for refractory angina pectoris. *Heart*. 2003;89:830-833.
9. Cohn PF. EECP – new data on possible mechanisms of action. *European Heart J*. 2001;22:1363-1364.
10. Stys T. Acute hemodynamic effects and angina improvement with enhanced external counterpulsation. *Angiology*. 2001; 52:653-658.
11. Michaels AD. Frequency and efficacy of repeat enhanced external counterpulsation for stable angina pectoris (from the International EECP Patient Registry). *Am J of Cardiology*. Feb 2005;95:394-397.
12. Bonetti PO, Holmes DR, Lerman A, Barsness GW, et al. Enhanced external counterpulsation for ischemic heart disease. *J Am College of Cardiology*. June 2003;41: 1918-1925.
13. Taguchi I, Ogawa K, Kanaya T, et al. Effects of enhanced external counterpulsation on hemodynamics and its mechanism – relation to neurohumoral factors. *Circ J Am Heart Assoc*. 2004. Nov;68:1030-1034.
14. Lawson WE, Hui JCK, Cohn PF, et al. Long-term prognosis of patients with angina treated with enhanced external counterpulsation: five-year follow-up study. *Clinical Cardiology*. April 2000; 254-258.
15. Parker JO. Angina pectoris: a review of emerging and current therapies. *Am J Man Care*. Oct 2004. 10 (11 suppl):S332-S338.
16. Yang EH, Barsness GW, Gersh BJ, Chandrasekaran K, Lerman A. Current and future treatment strategies for refractory angina. *Mayo Clinic Proc*. Oct 2004. 79(10): 1284-1292.
17. *The Physician's Guide to EECP Therapy*. Vol 15-0005. Vasomedical, Inc.; 2005:1-17.