Enhanced External Counterpulsation: Chronicle of a New Approach to the Therapy of Angina Pectoris

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

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The treatment of angina pectoris has undergone remarkable progress since the introduction of short-acting nitrates a century ago. These advances have occurred in increments concentrated in the last four decades and have paralleled elucidation of the pathophysiology of myocardial ischemia. The nitrates and subsequently introduced beta adrenergic blockers and calcium channel antagonists alleviate myocardial ischemia by reduction of myocardial oxygen demand (MVO_2) whereas myocardial revascularization by coronary artery bypass graft surgery or coronary angioplasty increases oxygen delivery to ischemic myocardium. Current therapy of angina consists of pharmacologic agents, adjunctive antithrombotic drugs, such as aspirin, vigorous risk factor reduction and, in selected patients, myocardial revascularization. This comprehensive approach has minimized the frequency of disabling angina and has allowed stabilization of all but a small minority of patients with unstable angina.

Despite these therapeutic advances, certain problems in the treatment of angina persist. Multidrug therapy, indicated in many patients, has potential disadvantages related to adverse effects, compliance, and expense. Revascularization is costly, angioplasty is afflicted by restenosis, and morbidity and mortality remain considerations with coronary bypass graft surgery. Further, not all patients with angina unresponsive to optimal medical therapy are candidates for either method of myocardial revascularization. Therefore, there remains a need for further innovation in antianginal therapy and EECP is a newly developed approach to this problem.

EECP is a noninvasive method for alleviating myocardial ischemia. Current results with EECP are an extension of clinical investigation initiated two decades ago with an earlier version of this

ABBREVIATIONS AND ACRONYMS

MVO_2	Myocardial oxygen demand
EECP	Enhanced external counterpulsation

modality which revealed promise in the treatment of angina[1] and demonstrated reduction of morbidity in patients with acute myocardial infarction complicated by mild left ventricular failure.[2] Although EECP has been approved by the FDA for the treatment of stable and unstable angina, acute myocardial infarction, and cardiogenic shock, the focus of recent clinical investigations has been treatment of angina refractory to current medical therapy. The physiologic rationale of EECP is both augmented perfusion to ischemic myocardium and reduction of MVO_2. To achieve these effects, EECP increases aortic blood pressure during diastole and reduces pressure in systole by sequential pneumatic compression and decompression of the lower limbs and buttocks which are encompassed in a series of cuffs. EECP is generally delivered in a course of 35 1-hour sessions administered 5 times per week. Current data, as presented in the papers in the October 1997 issue of *Cardiovascular Reviews & Reports* as well as this issue, support the efficacy of EECP in reducing both symptoms and myocardial ischemia in patients with angina unresponsive to current modes of therapy. The investigators involved in the evaluation of EECP have extended these findings in an ongoing series of studies aimed at clarifying mechanisms of efficacy, long term results, and the psychological impact of this noninvasive but transiently confining device. A current hypothesis concerning the mechanism of the sustained benefit of EECP in angina is the promotion of coronary collateral development.

In the previous issue of *CVR&R*, Lawson and colleagues reviewed the considerable combined experience with EECP in this country,[3] from the first report in 1992 to a current multicenter, in-progress trial of placebo (mild) EECP vs full EECP. The results of the latter study are awaited with interest because of the well established, potent placebo effect of a wide variety of interventions for the treatment of angina.[4] In their paper,[3] the authors describe a series of studies in which EECP not only reduced anginal symptoms refractory to medical therapy (as well as to revascularization in a large proportion of patients) but also improved objective measures of ischemia on treadmill testing and myocardial stress scintigraphy. These benefits were maintained over a follow up interval of 4–7 years in a majority of these high risk patients. Further investigation demonstrated that a therapeutic response to EECP is dependent on the presence of a patent conduit (either native coronary artery or bypass graft), presumably in order to transmit the augmented diastolic pressure to the distal coronary circulation. In addition, Doppler ultrasound has demonstrated that EECP increases measures of retrograde diastolic and antegrade systolic aortic flow, and the optimal range of diastolic augmentation has been identified for augmentation of the hemodynamic effects of EECP. Of considerable importance, the authors noted that no major morbidity or mortality has been observed in clinical trials of EECP, which have excluded patients with cardiac failure, aortic insufficiency, recent myocardial infarction, unstable angina, arrhythmias, peripheral vascular disease, and uncontrolled hypertension. The authors emphasized that the reported clinical trials of EECP encompass the entire spectrum of coronary patients, from those with single-vessel disease and normal left ventricular function to those with 3-vessel disease, stenosed bypass grafts, and impaired left ventricular function.

The psychological aspects of EECP were previously considered by Fricchione and coworkers.[5] They presented their extensive psychometric data that reveal improvement in depression scores in patients undergoing EECP irrespective of the effect of the treatment on myocardial ischemia. They noted that these salutary emotional effects contrast with the commonly negative psychosocial sequelae of revascularization procedures. These investigators also postulated that, in light of the positive association of depression with mortality from cardiac disease, the psychological gains of EECP may offer clinical advantages beyond its hemodynamic mechanisms.

In the first paper of this issue of *CVR&R*, Tartaglia presents 5 representative patients aged 45–79 years with refractory angina in whom revascularization procedures had failed. EECP was associated with both marked symptomatic improvement and objective evidence of decreased ischemia by either myocardial stress scintigraphy or exercise testing. Tartaglia further notes that, in his experience, 15 of 17 patients treated with EECP have responded favorably.

Soroff and colleagues review the history and physiologic rationale of EECP. They describe earlier versions of the device and beneficial clinical results in angina, myocardial infarction, and shock. Prior experimental studies have indicated that diastolic augmentation by external counterpulsation is related to the size of the vascular bed affected and is enhanced by sequential (distal to proximal) compression of the lower extremities. The current device utilizes both of these factors by compressing the lower extremities and buttocks in a sequenced mode for optimal diastolic augmentation and systolic unloading.

In the third paper of this series, Strobeck and coworkers describe the role of EECP in comprehensive cardiopulmonary care in their Heart-Lung

Center. The goals of EECP in this setting are to decrease symptoms of myocardial ischemia and reduce the need for interventional procedures. They utilize EECP in patients who have 1) failed myocardial revascularization and have at least one patent conduit in the coronary circulation; 2) 1- or 2-vessel coronary disease unsuitable for angioplasty or stent placement; and 3) 3-vessel disease unsuitable for bypass surgery. EECP is not indicated in left main coronary disease and in the presence of peripheral vascular disease. The authors urge caution in patients with left ventricular ejection fraction less than 30%. They report favorable effects on anginal symptoms in 41 of 45 patients treated with EECP, with objective evidence of decreased myocardial ischemia by myocardial stress scintigraphy. These results are exemplified by 3 detailed case histories in which EECP was utilized as an alternative to conventional revascularization in two of the patients and in one who had failed coronary bypass surgery. Symptoms were markedly reduced and ischemia on myocardial scintigraphy was notably improved.

This series of papers represents a commendable line of research into the benefits of EECP and a search for the underlying mechanisms. The investigators' studies extend from the angiographic and hemodynamic correlates of therapeutic efficacy to the psychological aspects of the intervention. They are well aware of the potential contribution of a placebo effect and are currently assessing this factor. The trials of EECP have largely involved high risk patients refractory to maximal medical therapy who are not candidates for myocardial revascularization. These studies have thus far demonstrated a high rate of success in alleviating anginal symptoms in association with objective evidence of decreased myocardial ischemia. Of particular interest is the achievement of sustained benefit from this intermittent, relatively short term method of therapy. These studies indicate the potential of EECP as an additional form of therapy for the treatment of angina. Further investigations of its mechanisms of efficacy are anticipated. Meanwhile, wider application of EECP in selected patients appears warranted.

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REFERENCES

1 Clap JC, Banas JS, Stickley LF, et al. Evaluation of sham and true external counterpulsation in patients with angina pectoris. *Circulation.* 1974;50:111–108.
2 Amsterdam EA, Banas J, Cartley JM, et al. Clinical assessment of external pressure circulatory assistance in acute myocardial infarction. *Am J Cardiol.* 1990;45:349–356.
3 Lawson WE, Cohn PF, Hui JCK, et al. Enhanced external counterpulsation: Review of U.S. clinical research to date. *CVR&R.* 1997;18:25–29.
4 Amsterdam EA, Wolfson S, Gorlin R. New aspects of the placebo response in angina pectoris (editorial). *Am J Cardiol.* 1969;24:305–306.
5 Fricchione GL, Hui J, Fife A, et al. Psychosocial aspects of enhanced external counterpulsation. *CVR&R.* 1997; 18:37–41.